

Flexible Manufacturing Facility for Biopharmaceuticals

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1.0 Abstract

Monoclonal antibodies (mAbs) have the potential to treat a wide range of diseases. They possess the ability to bind target molecules in a highly specific and effective manner. Recently, great technological advances have been made to enhance the therapeutic effects of these drugs, making treatment cheaper, easier, and more effective while allowing companies to profit significantly. As a Contract Manufacturing Organization (CMO) for these products, we offer the newest technology and many flexible options for producing these proteins. Our facility is designed to produce protein products in Chinese Hamster Ovary (CHO) cells, followed by modification and purification steps. We present the option to cleave smaller antigen binding fragments (Fab) from the mAb product, removing the crystallizable fragment (Fc) which can interfere with the binding specificity of the drug. We also offer the option for polyethylene glycosylation (PEGylation), which has been shown to improve the effectiveness of these drugs. The attachment of a polyethylene glycol (PEG) molecule to the protein enhances its circulation time in the human body so that less frequent doses are needed.

To demonstrate the capabilities of this flexible facility, we have modeled the production of an innovative PEGylated anti-TNF- α mAb. Celltech and Pfizer currently have similar products in Phase III clinical trials; and UCB Incorporated's Cimzia® recently received FDA approval for the first humanized PEGylated anti-TNF- α Fab' therapeutic protein. Many non-PEGylated TNF- α inhibitor mAbs are currently on the market to treat pathologies including rheumatoid arthritis and Crohn's disease. PEGylated products have a clear advantage over these drugs.

Our facility can produce up to 55 batches of protein product a year for a maximum yield of 993 kg. For economic analysis of this product, sales from the first year of Cimzia® were considered since this product is almost identical to the one being modeled. Producing at 75% of

the total design capacity, this facility has a NPV of \$1,319,592,100, an IRR of 33.51% and an ROI of 53.0%. This level of production would leave a significant amount of time remaining for other products to be manufactured as well. The additional products that the facility will produce will be mAbs of all forms (i.e. cleaved, uncleaved, PEGylated, non-PEGylated) that are protected under IP for small biotech firms that do not have the capital to build such facilities. Currently, small biotech firms are producing 81 mAbs and are looking to license production for their Phase III molecules. Clearly, this will become a very profitable CMO as we would be able to capture much of this demand. A major threat looming over the mAb market, however, is the production of small molecular inhibitors, which are currently in Phase I and Phase II clinical trials. Such molecules may be able to capture the full market since they would not only have significant delivery advantages over TNF- α inhibitors, which require injection, but also might have an enhanced side effect profile compared with biologics.

2.0 Introduction

Monoclonal antibodies (mAbs) are a class of biological agents currently used for therapeutics (see Figure 2.1). Their binding to target molecules is highly specific, which makes them useful for treating many human diseases including autoimmune and inflammatory conditions, cancers, and viral diseases (Sauer *et al.* 2000). Monoclonal antibodies are all identical to one another because they are produced by one single type of immune cell which are all clones of a single parent cell. While the mechanism by which mAbs achieve therapeutic effects is not very clear in all situations, some validated mechanisms include: the blocking or steric hindrance of a target antigen's function (i.e. tumor necrosis factor-alpha (TNF- α)), cytotoxicity to cells with specific receptors, and the inhibition of certain growth factor molecules (Bogard *et al.* 1989).

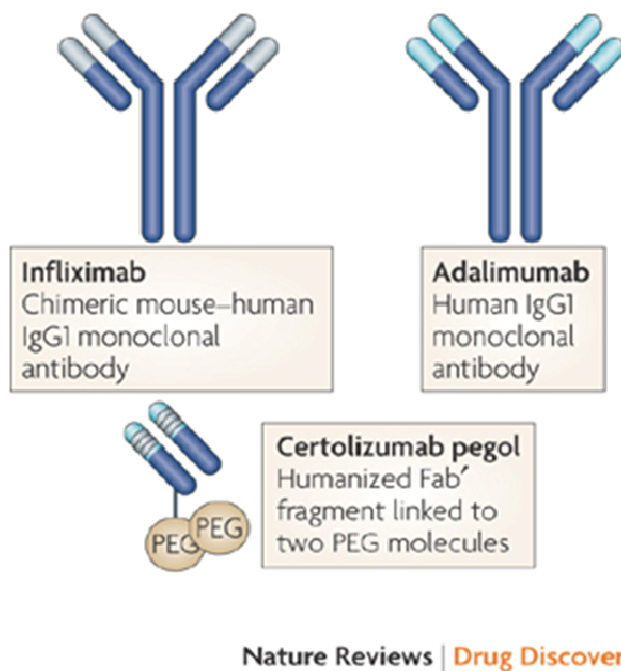


Figure 2.1: Three monoclonal antibodies currently used for treatment of Crohn's Disease. (Melmed *et.al.*, 2008)

TNF- α is a cytokine, or cell-signaling molecule, that is involved in inflammatory response pathways seen in patients with Crohn's, rheumatoid arthritis, and psoriatic arthritis. TNF- α is mainly produced by immune cells in response to bacteria, bacterial products, or other

inflammatory signals upstream. When TNF- α binds to TNF-R1, a membrane-bound TNF receptor found in almost all cells, it changes the conformation of the receptor and leads to an inflammatory response from the cell. As shown in Figure 2.2, anti-TNF- α antibodies bind to TNF- α and prevent it from binding to TNF-R1 through steric hindrance, inhibiting an inflammatory response (Magnani *et al.* 2005).

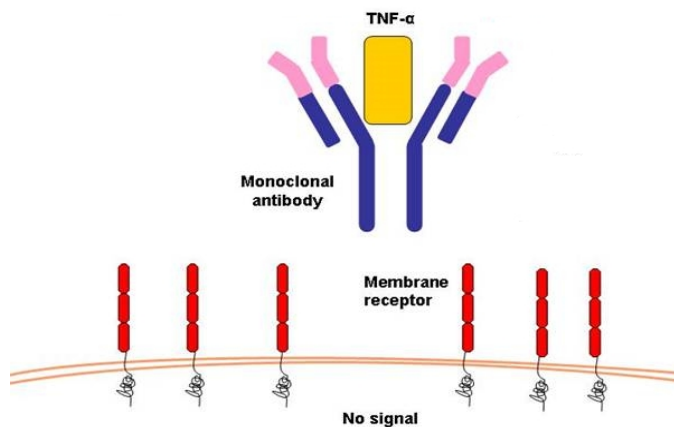


Figure 2.2: An Anti TNF- α binds to TNF- α , preventing it from signaling an inflammatory response through TNF-R1. (Magnani *et al.* 2005)

This company is a large Contract Research Organization (CRO) with plans to expand into contract manufacturing. The company specializes in biopharmaceuticals produced in mammalian cell culture systems, specifically monoclonal antibodies. The goal of the company was to design a facility capable of producing the next wave of mAb/Fab biopharmaceuticals, demonstrating the potential of this facility by modeling production of a humanized monoclonal antibody that inhibits TNF- α . This type of mAb is manufactured by enzymatically cleaving mAb fragments to form Fab fragments which are then polyethylene glycosylated (PEGylated), a process which attaches a polyethylene glycol (PEG) molecule to the protein. Since two-thirds of biopharmaceutical companies have revenues of less than one billion dollars, there is a great demand for Contract Manufacturing Organizations (CMOs) such as this. This is due to the fact

that many biopharmaceutical companies do not typically have the cash reserves to build a manufacturing facility outright.

This facility offers many levels of flexibility in the products that can be manufactured. For mAbs and other proteins, the Fc region must be enzymatically cleaved off, as it interferes with Fab binding to the TNF- α target. In the case of the anti-TNF- α drug that is modeled, the mAb is enzymatically cleaved with pepsin and PEGylated. Depending on whether the protein will be PEGylated or not, this facility is capable of cleaving 150 kDa mAbs with the enzyme papain to produce 50 kDa Fab fragments, or cleaving with the enzyme pepsin to produce 100 kDa F(ab')₂ molecules. F(ab')₂ molecules retain the hinge region disulfide bonds between the Fab and Fc fragments, which hold the two Fab fragments together when the 50 kDa Fc region is cleaved off (see Figure 2.3).

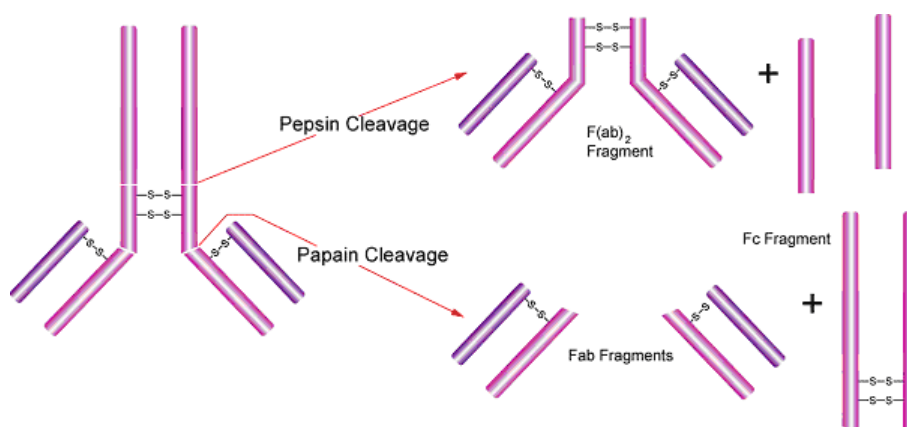


Figure 2.3: Depiction of a typical monoclonal antibody and its pepsin and papain cleavage products (Sigma-Aldrich).

These disulfide bonds holding the two Fab fragments together are then reduced using 2-Mercaptoethylamine-HCl (2-MEA) to yield two 50 kDa Fab' fragments (see Figure 2.4). Fab' fragments are Fab fragments with an additional cysteine attached, which is retained from the hinge region of the mAb. This cysteine contains a thiol group that can specifically react with the PEG molecule (see Figure 2.4). The PEGylation of the Fab product results in a very innovative

drug, as PEGylation has been shown to result in longer circulation time of the Fab in the bloodstream, reducing the amount and frequency of injections needed by patients (Filpula 2006).

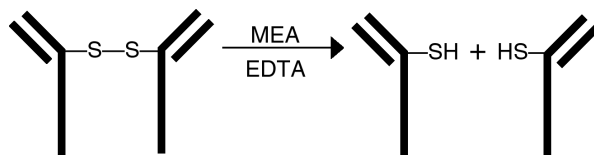


Figure 2.4: Reduction with 2-MEA (Thermo Scientific Pierce).

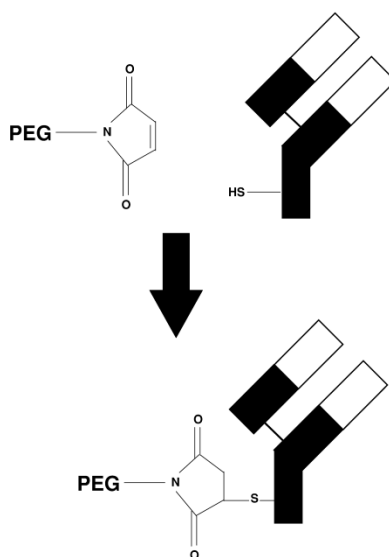


Figure 2.4: Schematic illustration of site-specific Fab' PEGylation through the attachment of PEG-maleimide to a thiol (Chapman 2002).

A Fab fragment that is not PEGylated has a blood half-life of 28 minutes, meaning that in this short amount of time it will lose half of its pharmacologic effect, and it has a hydrodynamic diameter of 6.0nm (Choi 2007). It has been experimentally determined that a particle with a hydrodynamic diameter less than or equal to 5.5 nm will be completely cleared from the body (Choi 2007). Above a molecular weight of 20 kDa, renal filtration decreases in favor of bile excretion, and above 50 kDa, hepatobiliary (liver) clearance dominates (Fishburn 2007). Since PEG molecules are highly hydrated, with two water molecules per ethylene glycol unit, they have a very large hydrodynamic diameter (Fishburn 2007). In experiments testing a range of molecular weights and configurations of PEG molecules, the optimal PEG to be added to a Fab'

fragment was found to be a 40 kDa branched molecule (Humphreys 2007). The hydrodynamic diameter of a 40 kDa PEG molecule has been proven to be about 20nm (Dhalluin 2005).

Attaching a single 40 kDa branched PEG molecule significantly increases the hydrodynamic diameter of the protein and almost doubles the molecular weight of the 40 kDa Fab' fragment, resulting in a 90 kDa product. Therefore, PEGylated proteins will be much greater in size and mass, remain in the body much longer, and allow for less frequent injections (Humphreys 2007).

In April of 2008, the FDA approved UCB's certolizumab pegol (Cimzia®), a product nearly identical to the biopharmaceutical being modeled. Cimzia® was the first humanized PEGylated anti-TNF- α Fab' therapeutic. Currently Cimzia® only has an indication to treat Crohn's disease, yet it is possible that it will be able to obtain an indication for rheumatoid arthritis in the future. Analyst expectations for the sales of Cimzia® were \$50 million for its launch year (Meldred 2008). Cimzia® is administered by a healthcare provider in 400 mg doses every four weeks via subcutaneous injections in the abdominal region or upper thigh. This differs from other biological TNF- α inhibitors on the market which must be intravenously injected.

For this facility, Chinese hamster ovary cells (CHO) were selected to produce anti-TNF- α antibodies. CHO cells are widely used in the expression of recombinant proteins, including monoclonal antibodies. Since they are mammalian cells, CHO cells are able to express and secrete a target antibody with proper post-translational modifications (PTMs), such as glycosylation and protein folding. Since the desired product is secreted, the purification is less complicated due to the fact that the intercellular proteins do not have to be separated out. CHO cells also grow quickly and can survive in dense populations, allowing for the recovery of concentrations of anti-TNF- α antibodies up to 5 g/L (Jayapal, Karthik P. *et al* 2007). CHO cells can also grow in suspension without serum, which allows for the cells to grow in large-scale stirred-tank bioreactors (>10,000 L) without the cost of expensive serums. In addition, the contamination of serum with viruses is a well known and established risk, which is why it will

not be used in this plant. Despite the testing of batches of serum, agents such as transmissible spongiform encephalopathies (TSEs) can escape detection and contaminate production cell cultures. The cells routinely used for production of biological medicines do not support the replication or amplification of TSEs. The only cell lines known to do so are of neuronal origin and use of such cells for production requires special justification (Castle 1998).

Safety and industrial acceptance were other important reasons for the selection of CHO cells to produce anti-TNF- α antibodies. CHO cells have been used in industry to produce biopharmaceuticals for 20 years, and have proven to be safe hosts for the synthesis of biologics. Their ability to consistently express stable and biologically active proteins is a chief reason why they are so commonly used. Another major benefit is that many of the major human pathogenic viruses, including HIV, influenza, polio, herpes, and measles, do not replicate inside CHO cells. This means that dangerous viruses will not propagate and thrive in these cells.

Since Massachusetts is currently a hotspot for biotechnology, this would be a practical and economic location for our manufacturing facility. Being on the East Coast, and particularly in the New England area, would put our facility at a great advantage. This location is close to cutting-edge academic research being done at local universities as well as suppliers, clients, and other companies with whom this facility might do business. This location would also decrease the cost associated with packaging and distributing our product. With the current shortage of cell-culture capacity and a large demand for antibody production in the biotech industry, a rapidly expanding state such as Massachusetts would give us the potential for expansion and collaboration with other companies in the future. The state government is also offering grants and other incentives to move into this area through the Massachusetts Development Emerging Technology Fund. Over the next ten years, Massachusetts plans to spend \$1 billion on subsidizing research and attracting and retaining biotech companies in the area. Many companies, both domestic and international, are taking advantage of this and in turn building

plants in Massachusetts (News Report 2005; Philippidis 2007). We also plan to take advantage of the opportunities that are available in the state of Massachusetts.

A potential threat to our facility would be the FDA approval of small molecule inhibitors of TNF- α . These molecules have the potential to have improved side effect profiles compared with biologics such as the ones being produced at our facility, which can cause dangerous infections. An oral inhibitor would also have delivery advantages over TNF- α inhibitors which require injections by healthcare providers. Table 2.1 below lists current compounds that are in Phase I and II clinical trials (Sheridan 2008).

Selected oral rheumatoid arthritis drugs in development

Developer	Compound	Mechanism	Status
Pfizer (New York)	CP-690,550	Janus kinase-3 (JAK3) inhibitor	Phase 2
Rigel	R788	Syk inhibitor	Phase 2
	R348	JAK3 inhibitor	Phase 1
Roche (Basel)/Toyama Chemical (Tokyo)	R7277 (T-5224)	Inhibits activator protein-1	Phase 1
Synta Pharmaceuticals (Lexington, Massachusetts)	Apilimod (STA-5326)	Inhibits production of interleukin-12, interleukin-23	Phase 2
Bristol-Myers Squibb (New York)/Pharmacoepia (Princeton, New Jersey)	BMS-582949	P38 kinase inhibitor	Phase 1 ^a
Pharmacoepia/Wyeth (Madison, New Jersey)	Unnamed	JAK3 inhibitor	Preclinical

^aIn phase 2 trials for psoriasis.

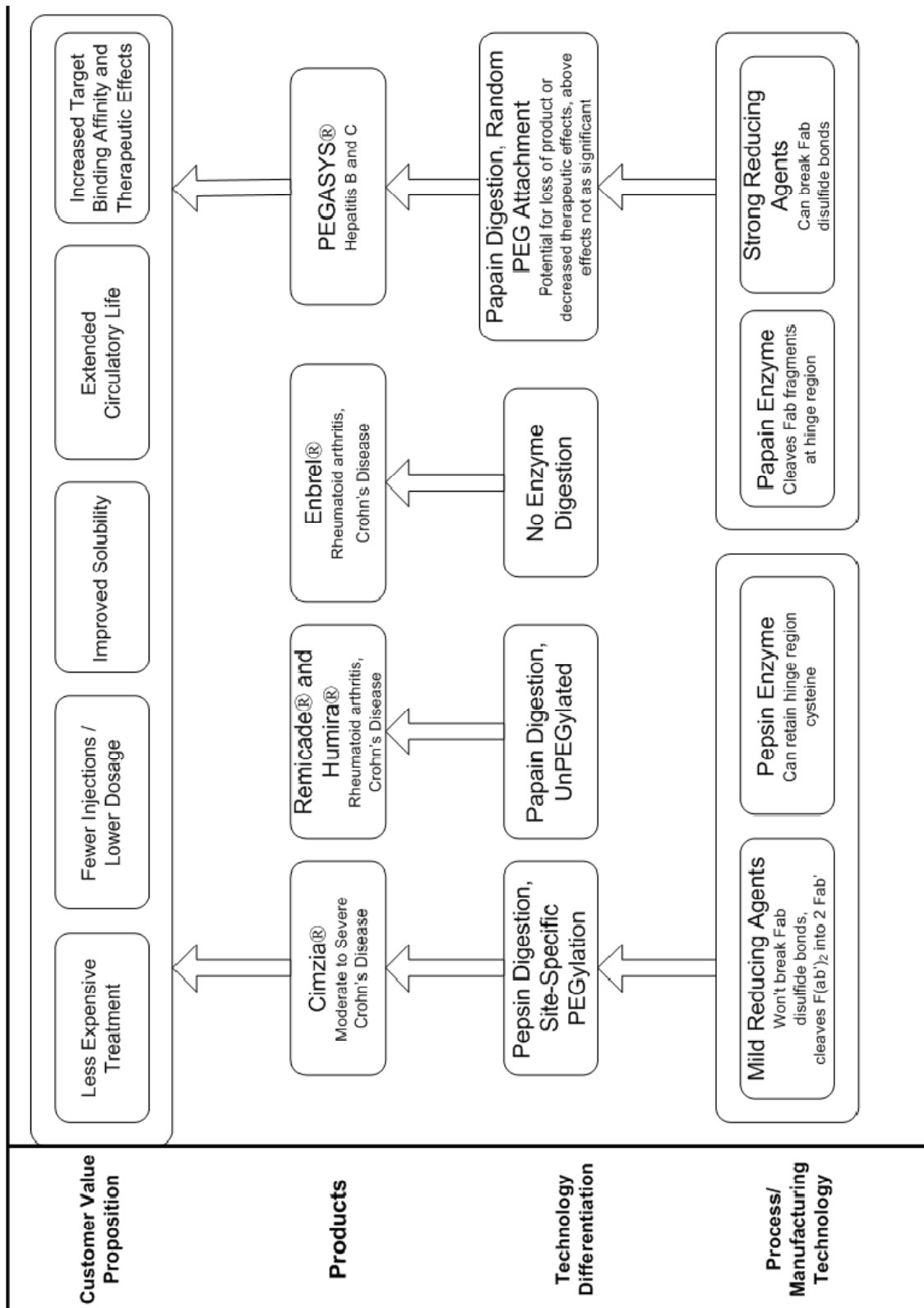
Table 2.1 Current small molecule inhibitors of TNF- α (Sheridan 2008).

2.1 Project Charter

Project Name	Humanized anti-TNF-alpha Antibody Production using a Flexible Biopharmaceutical Manufacturing Facility
Project Champions	Business Director of Biopharmaceutical Companies
Project Leaders	Ryan Dunn, Kevin Hsu, Melanie Hullings, Maria Lobikin
Specific Goals	Design a biopharmaceutical plant and a process to produce humanized monoclonal antibodies against TNF-alpha (Tumor Necrosis Factor)
Project Scope	<p>In-scope:</p> <ul style="list-style-type: none"> Enzymatic cleavage of antibody to produce Fab fragments <ul style="list-style-type: none"> Using papain digestion, antibody will be cleaved into two Fab fragments and an Fc fragment Using pepsin digestion, cleaving the antibody into an F(ab)₂' and Fc fragment PEGylation of fragments cleaved by pepsin for enhanced delivery <ul style="list-style-type: none"> Increases size, reducing renal clearance Masks product from immune response Meets current safety and health regulations Maintain profit margin Facility may be used to produce other biopharmaceuticals (i.e. non-cleaved, non-PEGylated antibodies) <p>Out-of-scope:</p> <ul style="list-style-type: none"> Process design of other biopharmaceuticals Cell line development Clinical Trials Distribution of product Research and development of monoclonal antibodies
Deliverables	<ul style="list-style-type: none"> Business opportunity assessment: <ul style="list-style-type: none"> How great is the business opportunity for biopharmaceutical contract manufacturing organizations? What is the market space for anti-TNF-alpha antibodies? Technical feasibility assessment: <ul style="list-style-type: none"> Is it technically feasible to manufacture anti-TNF-alpha antibodies on a large scale? Manufacturing capability assessment: <ul style="list-style-type: none"> Can this facility be built and can this process be executed without significant capital investment? Product life-cycle assessment: <ul style="list-style-type: none"> Would the facility and process satisfy current regulatory requirements?
Timeline	Facility and process design within 3 months

2.2 Technology-Readiness Assessment

Innovation Map: PEGylation



3.0 Concept Stage

3.1 Market and Competitive Analysis

While monoclonal antibodies (mAbs) made up only 20% of biologics sales in 2000, this segment is growing more rapidly than biologics in total. In 2007, total global monoclonal antibody sales reached \$26 billion and are forecast to almost double to \$49 billion by 2013.

While small molecule drug sales will continue to make up the majority of total market sales, the mAb market, with a compound annual growth rate (CAGR) of almost 11% will continue to grow at a much greater rate than their small molecule counterpart (DataMonitor 2008). With the expanding development and approval of mAbs comes the demand for production capacity by pharmaceutical companies.

As of today, there is a distinct shortage in cell culture capacity (Mallik 2006). There is currently a wealth of biopharmaceuticals that are either in Phase III of clinical trials or have been already approved. However, much of the world's cell-culture capacity is currently being utilized, and there is a lack of plant space for these newer drugs. Therefore, our plans to create a flexible biopharmaceutical manufacturing plant will help to address this demand. Not only is there a demand for manufacturing space in our facility, but there are also growing demands for the specific anti-TNF- α that the process described herein plans to manufacture.

3.1.1 Principle Competition Production Levels and Sales

Currently, the majority of drugs on the market which are similar to the anti-TNF- α protein being produced in this facility are non-PEGylated proteins which are very expensive and require frequent large-volume injections. Leading competitors for rheumatoid arthritis/Crohn's therapeutic proteins include J&J Centocor/Schering Plough's Remicade®, Abbott's Humira®, and Amgen/Wyeth's Enbrel®. As seen in Table 3.1 these products, as well as other monoclonal antibodies currently in the market) generate very large revenues. However, we can expect our product to generate similar revenues, as our product will be more effective and more appealing to patients than existing therapies. There are two known major competitors for this PEGylated product, as Celltech and Pfizer currently have a similar product in Phase III clinical trials and Cimzia just had the first humanized PEGylated anti-TNF- α Fab' protein approved by the FDA.

Production quantity for selected Mabs

BDS = bulk drug substance, total quantity < 10 tons/year

Product	Marketing companies	2007 revenue [US\$ million]	Estimated quantity [annual kg BDS]
Enbrel ^{*)}	Amgen / Wyeth	5.275	1.020
Remicade	J&J Centocor / Schering Plough	4.975	1.098
Rituxan / MabThera	Genentech / Roche	4.600	1.175
Herceptin	Genentech / Roche	4.046	1.015
Avastin	Genentech / Roche	3.424	873
Humira	Abbott	3.000	121
Xolair	Genentech / Novartis	613	246
Tysabri	Biogen Idec / Elan	343 [#]	51
Vectibix	Amgen	170	28

*) Enbrel is a Fc fusion protein: dose requirements, treatment cost, and production process is very similar to monoclonal antibodies

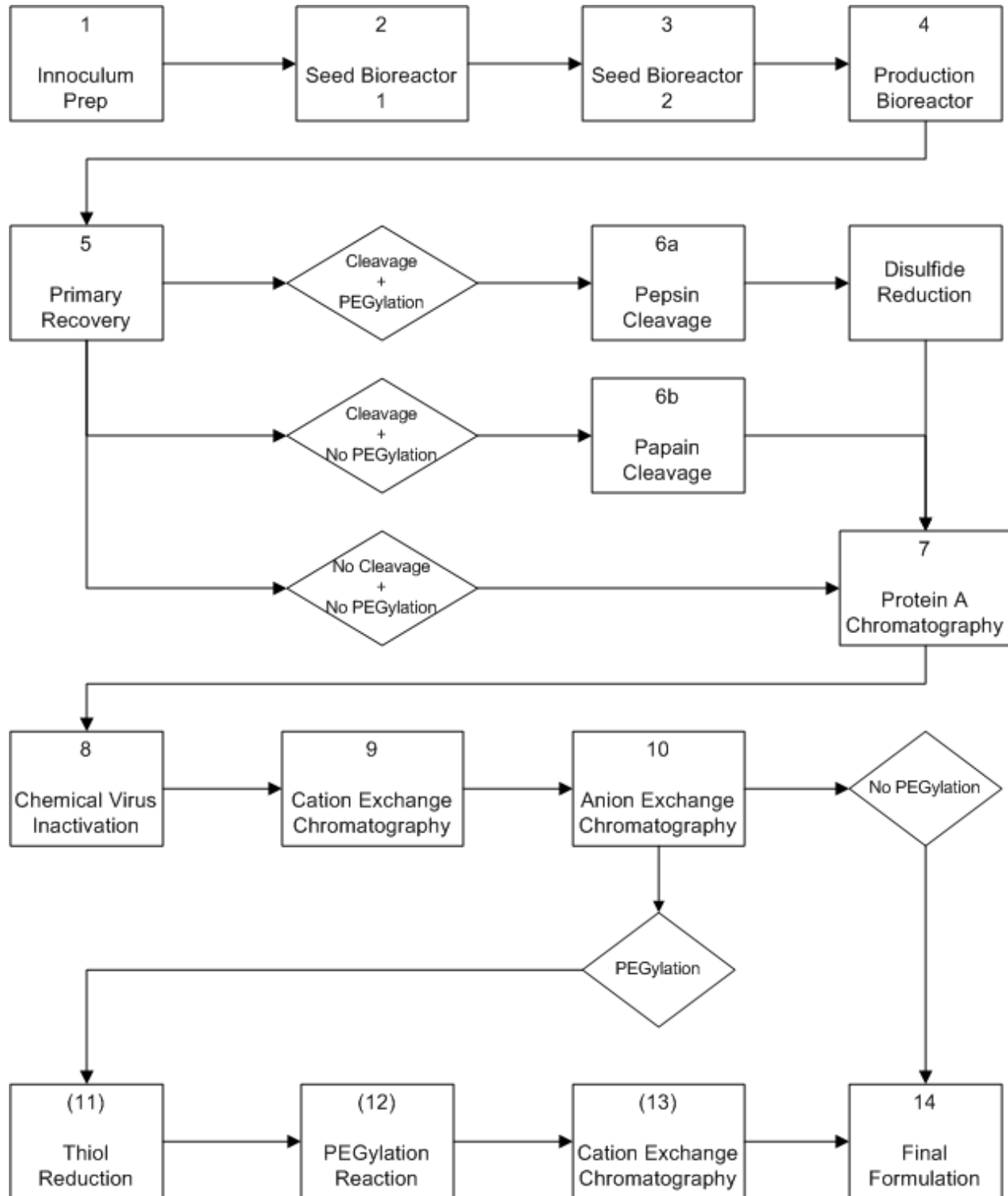
Table 3.1 Production levels and sales for principle competition (Jagschies 2009)

3.1.2 Customer Requirements

The customer requirements for this manufacturing facility fit a design concept that is new-unique-difficult (NUD). The primary customers of this CMO facility will be the biotechnology firms who wish to produce these drugs; and the primary focus of the facility should be to provide the technology required to produce the drugs these companies currently wish to manufacture. It is important that this facility is equipped with the newest technology in order to produce innovative drugs that fulfill the needs of the patients buying these products from the biotechnology companies. In either case, production capabilities must meet the requirements of the most current technologies, as well as anticipate the next generation of drugs. As there are available therapies for the same target as the drug being modeled, this facility focuses on providing flexible options in order to offer the capability to make innovative new products and replace existing ones. The PEGylated anti-TNF- α mAb being modeled will have enhanced effects over existing non-PEGylated products, as it will remain in the body longer, require smaller volume and less frequent injections, and potentially can be offered at a lower cost to the customer than the highly expensive therapies that exist in the market (Schlesselman, 2008).

3.2 Block Flow Diagram

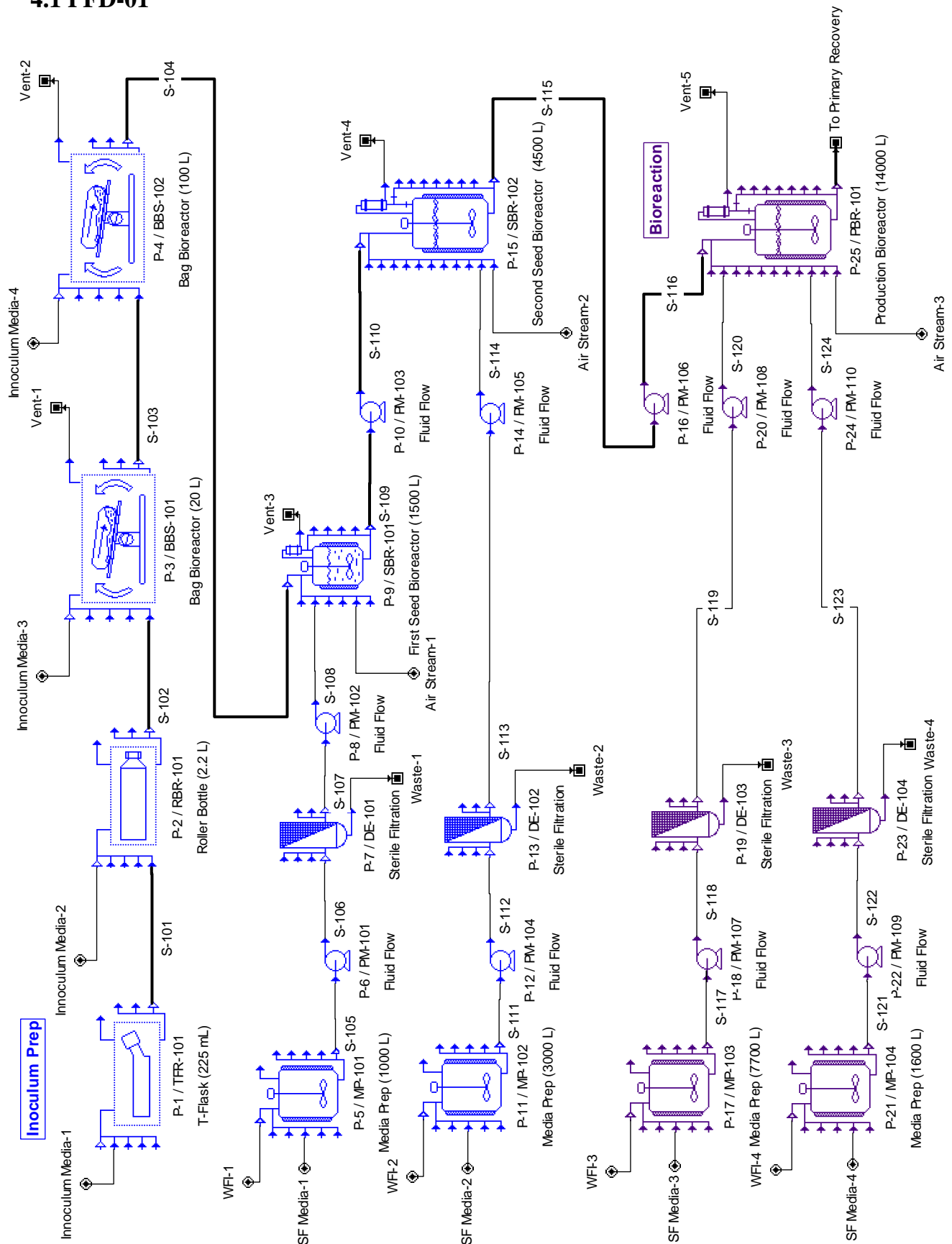
The diagram below depicts the overall process, as well as the three different possible production routes that can be implemented in creating the final product.



4.0 Process Flow Diagrams

The following pages contain the process flow diagrams and material balances describing the flexible manufacturing facility for the production of monoclonal antibodies. Flexibility in the facility is provided by the ability to create three different products through the utilization and/or bypass of certain unit(s). The final monoclonal antibody produced can be either cleaved and PEGylated, cleaved and not PEGylated, or neither cleaved nor PEGylated (see block flow diagram, p.11).

4.1 PFD-01

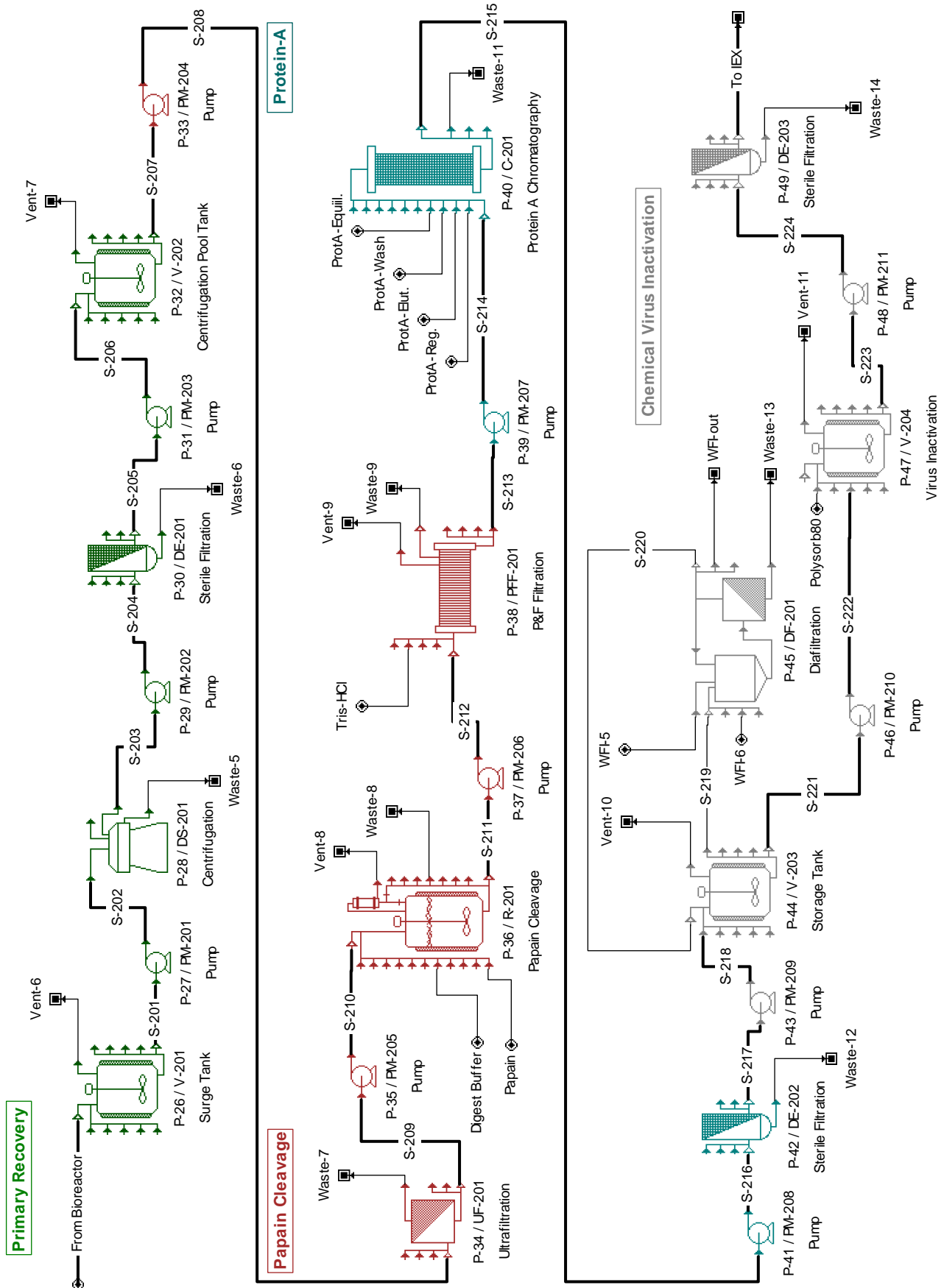


4.1.1 Overall Material Balance PFD-01

OVERALL COMPONENT BALANCE (kg/batch)					
COMPONENT	INITIAL	INPUT	OUTPUT	FINAL	OUT-IN
Amino Acids	0.00	34.00	3.49	0.20	- 30.32
Biomass	0.00*	0.00	167.26	0.00	167.26
Carbon Dioxide	0.00	0.00	338.58	0.29	338.87
Dead Biomass	0.00	0.00	17.14	0.00	17.14
Glucose	0.00	143.88	14.75	0.83	- 128.30
Glutamine	0.00	16.64	1.71	0.10	- 14.84
Inorganic Salts	0.00	348.53	35.72	2.01	- 310.80
Lactate	0.00	0.00	118.59	0.00	118.59
MAB	0.00	0.00	34.32	0.00	34.32
Nitrogen	30.74	16763.30	16776.38	17.66	0.00
Other Media Components	0.00	3.01	0.31	0.02	- 2.69
Oxygen	9.33	5089.01	4605.18	4.94	- 488.22
Phosphoric Acid	0.00	233.54	233.54	0.00	0.00
Sodium Hydroxide	0.00	44.51	44.51	0.00	0.00
Vitamins	0.00	1.42	0.15	0.01	- 1.27
Water	0.00	0.00	300.26	0.00	300.26
WFI	0.00	41604.18	41593.90	10.28	0.00
TOTAL	40.07	64282.02	64285.77	36.32	0.00

*Refers to a low inoculum concentration of initial biomass at the start of the process.

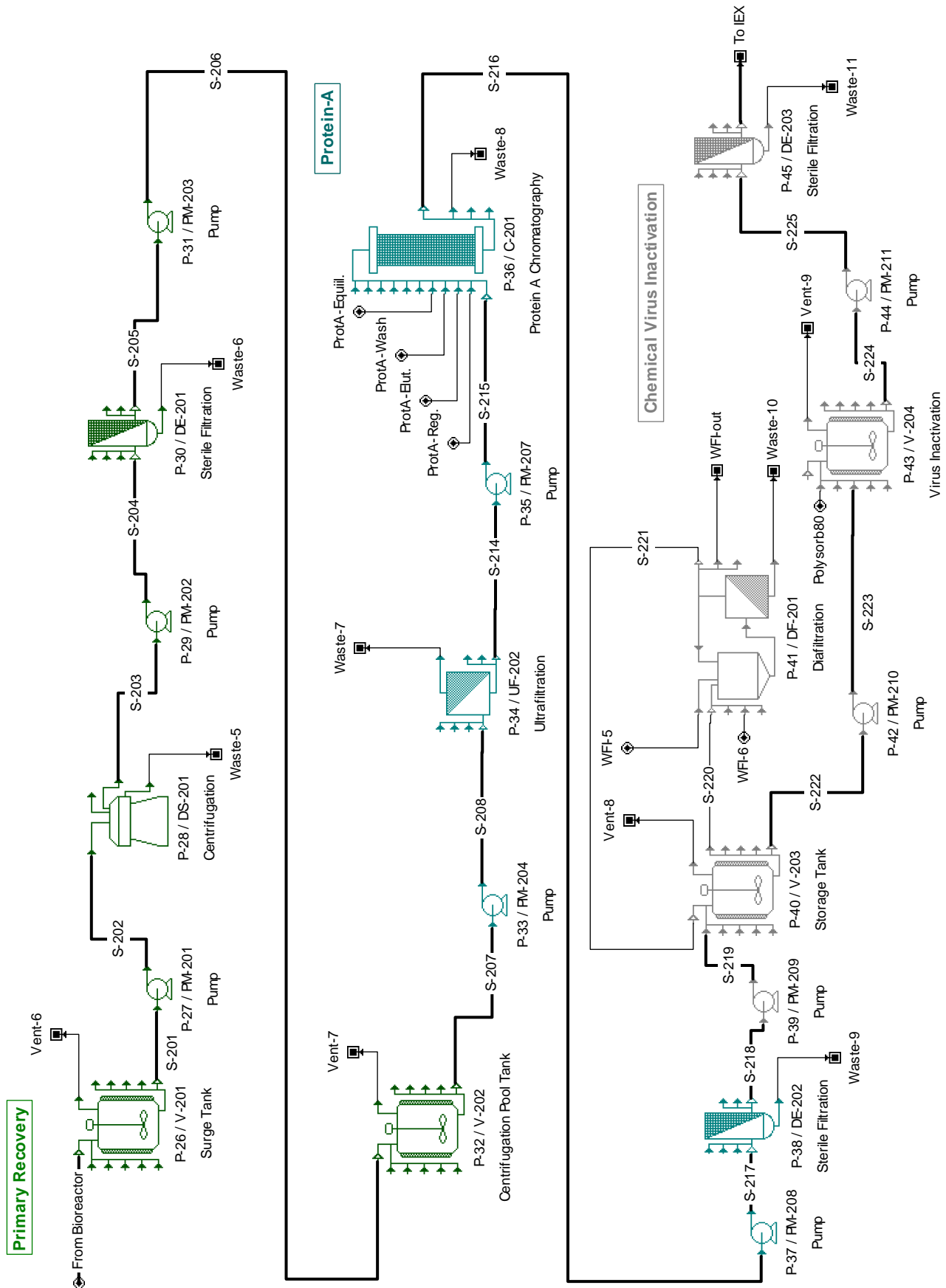
4.2 PFD-02 (for product that is cleaved and not PEGylated)



4.2.1 Overall Material Balance PFD-02

OVERALL COMPONENT BALANCE (kg/batch)					
COMPONENT	INITIAL	INPUT	OUTPUT	FINAL	OUT-IN
Amino Acids	0.00	3.49	3.49	0.00	0.00
Acetic-Acid	0.00	15.80	15.80	0.00	0.00
Biomass	0.00	167.26	167.26	0.00	0.00
Cysteine-HCl	0.00	5.45	5.45	0.00	0.00
Dead Biomass	0.00	17.14	17.14	0.00	0.00
EDTA, Disodium	0.00	9.02	9.02	0.00	0.00
EDTA, Sodium	0.00	11.59	11.59	0.00	0.00
Glucose	0.00	14.75	14.75	0.00	0.00
Glutamine	0.00	1.71	1.71	0.00	0.00
Impurities	0.00	0.00	0.54	0.00	0.54
Inorganic Salts	0.00	35.72	35.72	0.00	0.00
Lactate	0.00	118.59	118.59	0.00	0.00
MAB	0.00	34.32	4.87	0.00	- 29.45
mAb Fab	0.00	0.00	19.09	0.00	19.09
mAb Fc	0.00	0.00	9.82	0.00	9.82
Nitrogen	30.56	13.97	13.80	30.73	0.00
Other Media Components	0.00	0.31	0.31	0.00	0.00
Oxygen	9.28	4.24	4.19	9.33	0.00
Papain	0.00	1540.43	1540.43	0.00	0.00
Phosphoric Acid	0.00	240.08	240.08	0.00	0.00
Polysorbate 80	0.00	0.10	0.10	0.00	0.00
Sodium Chloride	0.00	5.79	5.79	0.00	0.00
Sodium Citrate	0.00	2.85	2.85	0.00	0.00
Sodium Hydroxide	0.00	87.33	87.33	0.00	0.00
Sodium Phosphate	0.00	4.20	4.20	0.00	0.00
TRIS Base	0.00	5.79	5.79	0.00	0.00
TRIS HCl	0.00	224.16	224.16	0.00	0.00
Vitamins	0.00	0.15	0.15	0.00	0.00
Water	0.00	19696.99	19696.99	0.00	0.00
WFI	0.00	48806.42	48806.42	0.00	0.00
TOTAL	39.84	71067.63	71067.41	40.06	0.00

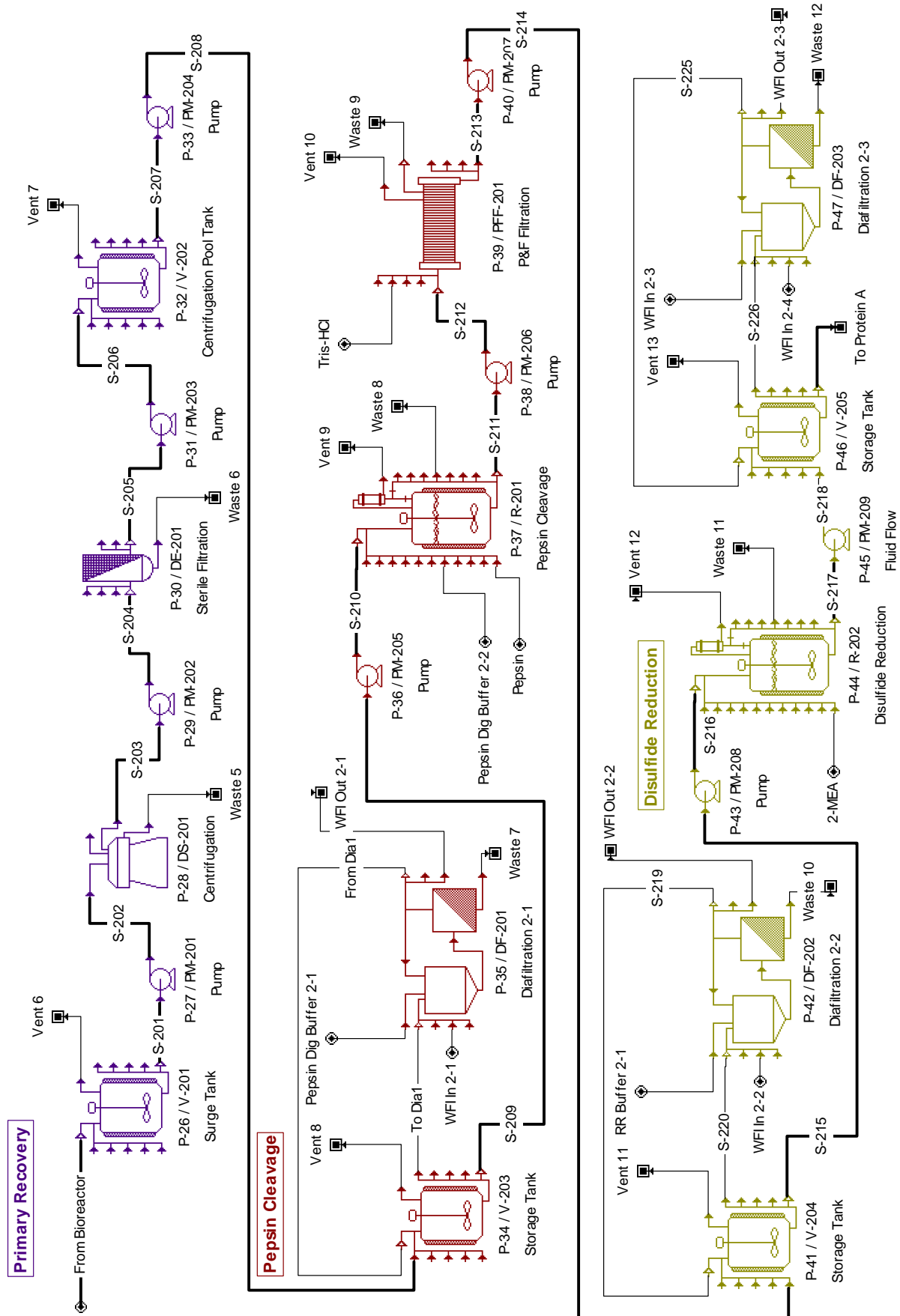
4.3 PFD-02a (for product that is neither cleaved nor PEGylated)



4.3.1 Overall Material Balance PFD-02a

OVERALL COMPONENT BALANCE (kg/batch)					
COMPONENT	INITIAL	INPUT	OUTPUT	FINAL	OUT-IN
Amino Acids	0.00	0.29	0.29	0.00	0.00
Acetic-Acid	0.00	67.11	67.11	0.00	0.00
Biomass	0.00	184.88	184.88	0.00	0.00
Dead Biomass	0.00	18.94	18.94	0.00	0.00
EDTA, Sodium	0.00	49.20	49.20	0.00	0.00
Glucose	0.00	1.23	1.23	0.00	0.00
Glutamine	0.00	0.14	0.14	0.00	0.00
Impurities	0.00	0.00	0.95	0.00	0.95
Inorganic Salts	0.00	2.98	2.98	0.00	0.00
Lactate	0.00	131.08	131.08	0.00	0.00
mAb	0.00	37.94	36.98	0.00	- 0.954
Nitrogen	33.52	18.21	17.81	33.92	0.00
Other Media Components	0.00	0.03	0.03	0.00	0.00
Oxygen	10.18	5.53	5.41	10.30	0.00
Phosphoric Acid	0.00	199.19	199.19	0.00	0.00
Polysorbate 80	0.00	0.09	0.09	0.00	0.00
Sodium Chloride	0.00	24.60	24.60	0.00	0.00
Sodium Citrate	0.00	12.09	12.09	0.00	0.00
Sodium Hydroxide	0.00	112.27	112.27	0.00	0.00
TRIS Base	0.00	24.60	24.60	0.00	0.00
TRIS HCl	0.00	73.81	73.81	0.00	0.00
Vitamins	0.00	0.01	0.01	0.00	0.00
Water	0.00	19728.62	19728.62	0.00	0.00
WFI	0.00	80412.48	80412.48	0.00	0.00
TOTAL	43.69	101105.34	101104.81	44.22	0.00

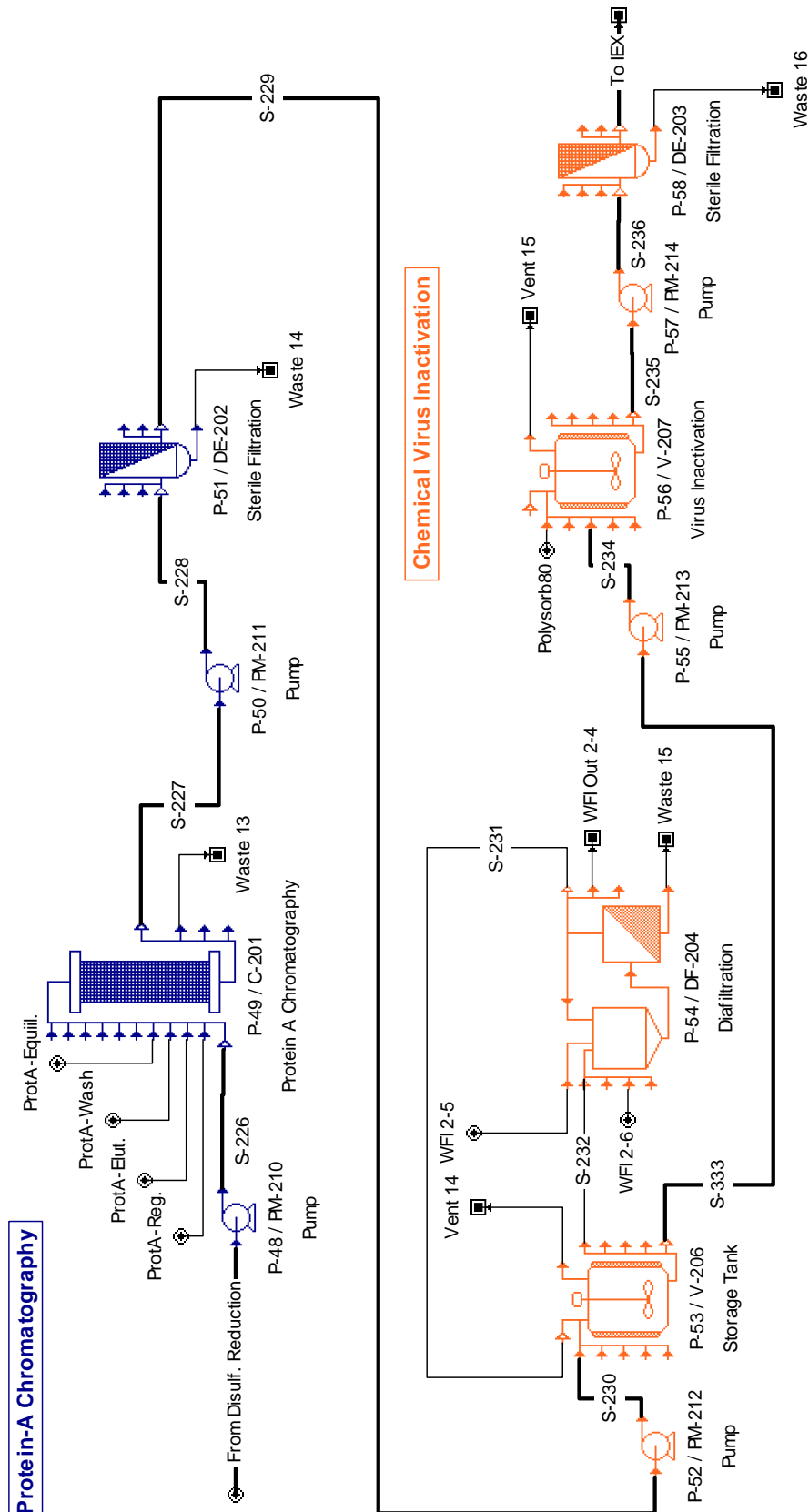
4.4 PFD-03a (for product that is cleaved and PEGylated)



4.4.1 Overall Material Balance PFD-03a

OVERALL COMPONENT BALANCE (kg/batch)					
COMPONENT	INITIAL	INPUT	OUTPUT	FINAL	OUT-IN
2-MEA	0.00	0.08	0.08	0.00	0.00
Amino Acids	0.00	3.49	3.49	0.00	0.00
Biomass	0.00	167.26	167.26	0.00	0.00
Dead Biomass	0.00	17.14	17.14	0.00	0.00
EDTA, Sodium	0.00	432.20	432.20	0.00	- 0.00
F(ab') ₂ Fragments	0.00	0.00	0.92	0.00	0.92
Glucose	0.00	14.75	14.75	0.00	0.00
Glutamine	0.00	1.71	1.71	0.00	0.00
HCl	0.00	0.02	0.02	0.00	0.00
Impurities	0.00	0.00	0.98	0.00	0.98
Inorganic Salts	0.00	35.77	35.77	0.00	0.00
Lactate	0.00	118.59	118.59	0.00	- 0.000
mAb	0.00	34.32	4.77	0.00	- 29.55
mAb Fab	0.00	0.00	14.31	0.00	14.31
mAb Fc	0.00	0.00	13.33	0.00	13.33
Nitrogen	49.10	33.83	34.81	48.11	- 0.00
Other Media Components	0.00	0.31	0.31	0.00	0.00
Oxygen	14.91	10.27	10.57	14.61	- 0.00
Pepsin	0.00	1540.43	1540.43	0.00	0.00
Phosphoric Acid	0.00	400.60	400.60	0.00	0.00
Sodium Acetate	0.00	51.17	51.17	0.00	- 0.00
Sodium Chloride	0.00	12965.87	12965.87	0.00	- 0.00
Sodium Hydroxide	0.00	93.39	93.39	0.00	0.00
Sodium Phosphate	0.00	4082.05	4082.05	0.00	- 0.00
TRIS HCl	0.00	206.78	206.78	0.00	0.00
Vitamins	0.00	0.15	0.15	0.00	0.00
Water	0.00	15220.82	15220.82	0.00	- 0.00
WFI	0.00	75680.08	75680.08	0.00	- 0.00
TOTAL	64.00	111111.03	111112.31	62.73	0.00

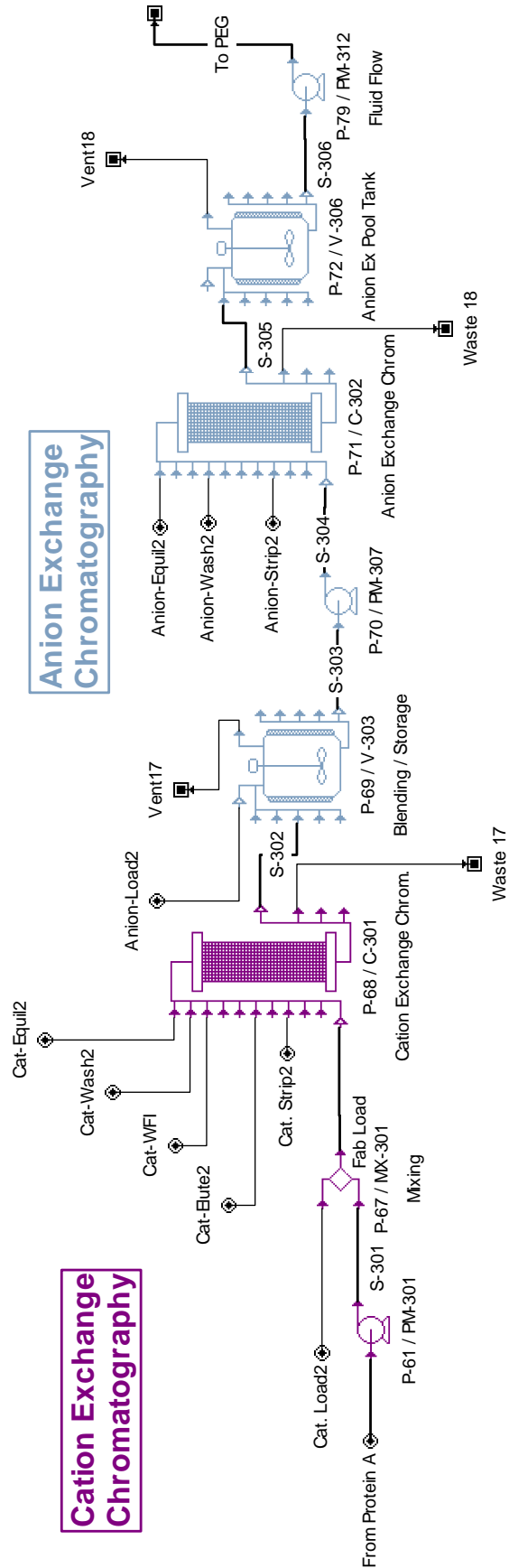
4.5 PFD-03b (for product that is cleaved and PEGylated)



4.5.1 Overall Material Balance PFD-03b

OVERALL COMPONENT BALANCE (kg/batch)					
COMPONENT	INITIAL	INPUT	OUTPUT	FINAL	OUT-IN
2-MEA	0.00	0.01	0.01	0.00	0.00
Amino Acids	0.00	0.00	0.00	0.00	0.00
Acetic-Acid	0.00	0.51	0.51	0.00	0.00
Dead Biomass	0.00	0.01	0.01	0.00	0.00
EDTA, Sodium	0.00	25.57	25.57	0.00	0.00
Glucose	0.00	0.01	0.01	0.00	0.00
Glutamine	0.00	0.00	0.00	0.00	0.00
Impurities	0.00	0.23	0.23	0.00	0.00
Inorganic Salts	0.00	0.03	0.03	0.00	0.00
Lactate	0.00	0.08	0.08	0.00	0.00
mAb	0.00	0.02	0.02	0.00	0.00
MAb Fab Fragments	0.00	14.31	14.31	0.00	0.00
MAb Fc Fragments	0.00	0.23	0.23	0.00	0.00
Nitrogen	5.21	5.58	5.43	5.37	0.00
Other Media Components	0.00	0.00	0.00	0.00	0.00
Oxygen	1.58	1.70	1.65	1.63	0.00
Phosphoric Acid	0.00	82.73	82.73	0.00	0.00
Polysorbate 80	0.00	0.09	0.09	0.00	0.00
Sodium Acetate	0.00	0.19	0.19	0.00	0.00
Sodium Chloride	0.00	756.15	756.15	0.00	0.00
Sodium Citrate	0.00	0.09	0.09	0.00	0.00
Sodium hydroxide	0.00	50.31	50.31	0.00	0.00
Sodium Phosphate	0.00	238.00	238.00	0.00	0.00
TRIS Base	0.00	0.19	0.19	0.00	0.00
TRIS HCl	0.00	3.50	3.50	0.00	0.00
Vitamins	0.00	0.00	0.00	0.00	0.00
Water	0.00	7460.49	7460.49	0.00	0.00
WFI	0.00	15557.20	15557.20	0.00	0.00
TOTAL	6.79	24197.25	24197.04	7.00	0.00

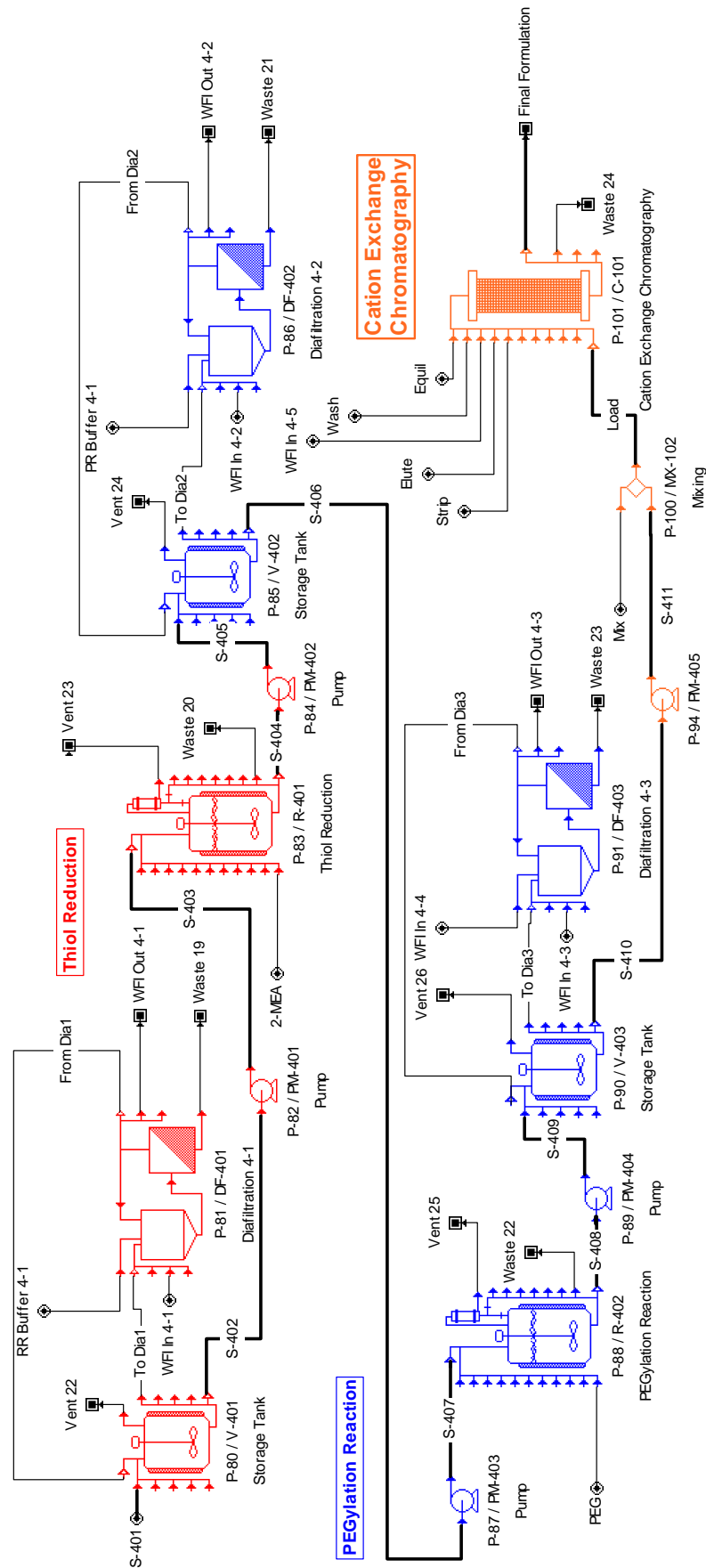
4.6 PFD-04*



4.6.1 Overall Material Balance PFD-04

OVERALL COMPONENT BALANCE (kg/batch)					
COMPONENT	INITIAL	INPUT	OUTPUT	FINAL	OUT-IN
2-MEA	0.00	0.00	0.00	0.00	0.00
Amino Acids	0.00	0.00	0.00	0.00	0.00
Acetic-Acid	0.00	0.01	0.01	0.00	0.00
EDTA, Sodium	0.00	0.67	0.67	0.00	0.00
Glucose	0.00	0.00	0.00	0.00	0.00
Glutamine	0.00	0.00	0.00	0.00	0.00
Impurities	0.00	0.09	0.09	0.00	0.00
Inorganic Salts	0.00	0.00	0.00	0.00	0.00
Lactate	0.00	0.00	0.00	0.00	0.00
mAb Fab Fragments	0.00	14.31	14.31	0.00	0.00
MES	0.00	104.52	104.52	0.00	0.00
Nitrogen	22.80	0.00	20.52	2.28	0.00
Other Media Components	0.00	0.00	0.00	0.00	0.00
Oxygen	6.92	0.00	6.23	0.69	0.00
Phosphoric Acid	0.00	84.26	84.26	0.00	0.00
Polysorbate 80	0.00	0.09	0.09	0.00	0.00
Sodium Acetate	0.00	0.01	0.01	0.00	0.00
Sodium Chloride	0.00	102.81	102.81	0.00	0.00
Sodium Hydroxide	0.00	48.08	48.08	0.00	0.00
Sodium Phosphate	0.00	6.36	6.36	0.00	0.00
TRIS Base	0.00	18.71	18.71	0.00	- 0.000
TRIS HCl	0.00	0.08	0.08	0.00	0.00
Vitamins	0.00	0.00	0.00	0.00	0.00
Water	0.00	28322.06	28322.06	0.00	0.00
WFI	0.00	22975.18	22975.18	0.00	- 0.000
TOTAL	29.72	51677.23	51703.98	2.97	0.00

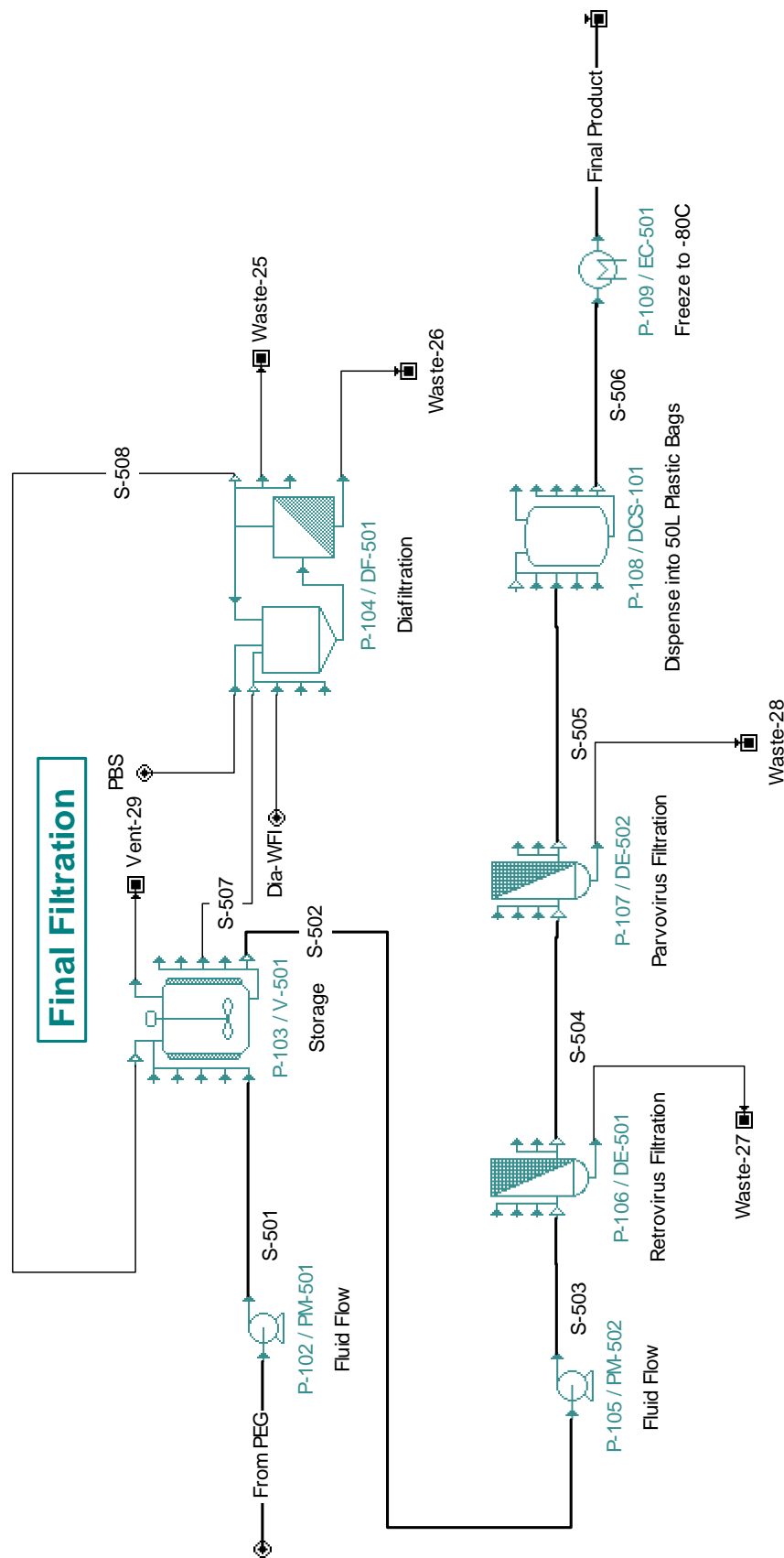
4.7 PFD-05



4.7.1 Overall Material Balance PFD-05

OVERALL COMPONENT BALANCE (kg/batch)					
COMPONENT	INITIAL	INPUT	OUTPUT	FINAL	OUT-IN
2-MEA	0.00	8.90	8.90	0.00	0.00
EDTA, Disodium	0.00	2.21	2.21	0.00	0.00
EDTA, Sodium	0.00	5.64	5.64	0.00	0.00
Impurities	0.00	0.00	0.00	0.00	0.00
mAb Fab Fragments	0.00	12.89	0.64	0.00	- 12.242
MacroCap SP	2026.87	0.00	2026.87	0.00	0.00
MES	0.00	0.46	0.46	0.00	0.00
Nitrogen	14.53	5.63	5.36	14.79	- 0.000
Oxygen	4.41	1.71	1.63	4.49	- 0.000
PEG	0.00	225.48	216.17	0.00	- 9.304
PEGylated mAb Fragments	0.00	0.00	20.93	0.00	20.93
Phosphate	0.00	109.60	109.60	0.00	0.00
Phosphoric Acid	0.00	231.33	231.33	0.00	0.00
Reduced mAb Fab Fragments	0.00	0.00	0.61	0.00	0.61
Sodium Chloride	0.00	103.85	103.85	0.00	- 0.000
Sodium hydroxide	0.00	76.62	76.62	0.00	0.00
TRIS Base	0.00	15.25	15.25	0.00	0.00
Water	0.00	23242.95	23242.95	0.00	0.00
WFI	0.00	43496.39	43496.39	0.00	- 0.000
TOTAL	2045.81	67538.89	69565.42	19.29	0.00

4.8 PFD-06



4.8.1 Overall Material Balance PFD-06

OVERALL COMPONENT BALANCE (kg/batch)					
COMPONENT	INITIAL	INPUT	OUTPUT	FINAL	OUT-IN
Impurities	0.00	0.00	0.00	0.00	0.00
KCl	0.00	0.00	0.00	0.00	0.00
KH ₂ PO ₄	0.00	0.00	0.00	0.00	0.00
mAb Fab Fragments	0.00	0.00	0.00	0.00	0.00
Na ₂ HPO ₄	0.00	0.42	0.42	0.00	0.00
Nitrogen	1.24	0.43	0.43	1.24	0.00
Oxygen	0.38	0.13	0.13	0.38	0.00
PEGylated mAb Fragments	0.00	18.89	18.42	0.00	- 0.472
Phosphate	0.00	0.24	0.24	0.00	0.00
Phosphoric Acid	0.00	30.85	30.85	0.00	0.00
Sodium Chloride	0.00	10.32	10.32	0.00	0.00
Sodium Hydroxide	0.00	8.38	8.38	0.00	0.00
Water	0.00	5968.23	5968.23	0.00	0.00
WFI	0.00	4301.37	4301.85	0.00	0.47
TOTAL	1.61	10339.26	10339.26	1.61	0.00

5.0 Production Process Description

5.1 Preliminary Steps (BFD-01)

5.1.1 Buffer Preparation

Buffers needed for the process are prepared in sterile disposable containers located in a buffer prep room. This greatly aids in quality and compliance. Disposable containers eliminate the requirements for clean in place (CIP) and steam in place (SIP) validation (See Appendix A), especially in-process quality control (QC) documentation, service, and calibration requirements. In addition, disposables eliminate the possibility of residual carryover from batch to batch and contamination with CIP agents.

Buffers, in most cases, will be diluted in-line with water for injection (WFI). Once at full volume, the buffers will be tested and verified to make sure that they are at the proper pH. If the buffers are incorrectly prepared, they will need to be adjusted before a calculated amount is placed in individual transfer bags for use in the process. Before any buffer is added to any of the bioreactors, it must first pass through a 0.2 µm sterile filter to ensure that any bacteria or other contaminants have been properly removed.

5.1.2 Media Preparation

EX-CELL[®] ACF CHO Serum Free Medium purchased from Sigma-Aldrich[®] is used exclusively for this process. For the initial inoculum steps in which small volumes of media are needed, a liquid form of the media purchased directly from Sigma-Aldrich[®] is used, while a powdered version of the media mixed with WFI in storage/mixing tanks is used for the seed bioreactor sections through the production bioreactor section. The solution will be 2% by mass powdered media and 98% by mass WFI. Both forms of media come from the same lot of material so the cells will experience no changes due to the use of powdered versus liquid media as they travel through the process. Before any media is added to any of the bioreactors, it must

first pass through a 0.2 μm sterile filter to ensure that any bacteria or other contaminants have been properly removed.

5.2 Inoculum Prep Section (BFD-01)

5.2.1 T-Flasks (TFR-101)

First, a provided vial of cells from R&D is removed from a freezer and stored in a biosafety cabinet until fully thawed. Once thawed, the cells are resuspended in fresh media and centrifuged. The supernatant is discarded. Twenty 225 mL Nunc non-treated, sterile t-flasks are then each initially inoculated with one million of these cells and 106 mL of serum free media using serological pipettes. Each t-flask thus has a working volume of 50% to allow for proper agitation as recommended by Nunc International from which these t-flasks are being purchased. The t-flasks are stored on rockers in an incubator at 37°C over the course of 4 days. The media will equilibrate around a neutral pH of 7.0. However, this is considered to be an uncontrolled system so the pH may range anywhere from 6.5 to 7.5. The incubator allows for necessary aeration so that the cells can obtain the oxygen they need for growth. However, limitations due to oxygen are expected.

5.2.2 Roller Bottles (RBR-101)

Next, the cultures from the t-flasks are pooled together in a sterile glass vessel. A sterile serological pipette is used to transfer about 196 mL of culture to each of eleven 2.2 L standard roller bottles. An additional 800 mL of fresh serum free media is added to each of these bottles such that each roller bottle has a working volume of 50% to allow for proper agitation as recommended by the manufacturer Nunc International. The roller bottles are stored in a rotational incubator at 37°C over the course of 4 days. Again, the media will equilibrate around a neutral pH of 7.0 despite this being an uncontrolled system with a pH that may range anywhere

from 6.5 to 7.5. The incubator allows for necessary aeration so that the cells can obtain the oxygen they need for growth. However, limitations due to oxygen are expected.

5.2.3 Bag Bioreactor 1 (BBS-101)

The cultures are then pooled two at a time in a sterile glass vessel. 1.38 L of culture are transferred from this vessel with connected tubing via a peristaltic pump on a movable cart to each of eight 20 L bag bioreactors. An additional 7.5 L of fresh serum free media is added to each of these disposable bags such that each has a working volume of 50% to allow for proper mixing as recommended by Sartorius Stedim Biotech. Process control is achieved through disposable optical chemical pH and dissolved oxygen (DO) sensors with feedback control of both values being available for the process. The temperature is kept at 37°C over the course of 4 days. The pH is maintained at 7.0, which is recommended for CHO cell growth, while the dissolved oxygen level is maintained at 50%. The bag bioreactor allows for necessary aeration so that the cells can obtain the oxygen they need for growth.

5.2.4 Bag Bioreactor 2 (BBS-102)

Next, the cultures are transferred from the eight 20 L bag bioreactors via a peristaltic pump on a movable cart to seven 100 L bag bioreactors. An additional 35.7 L of fresh serum free media is added to each of these disposable bags such that each has a working volume of 50% to allow for proper agitation as recommended by Sartorius Stedim Biotech. Process control is achieved through disposable optical chemical pH and DO sensors with feedback control of both values being available for the process. The temperature is kept at 37°C over the course of 4 days. The pH is maintained at 7.0, while the dissolved oxygen level is maintained at 50%. The package allows for necessary aeration so that the cells can obtain the oxygen they need for growth.

5.3 Seed Bioreactor Sections (BFD-02 / BFD-03)

5.3.1 Seed Bioreactor 1 (SBR-101)

Following the 4 days of time in the second set of bag bioreactors, the cells are transferred from the seven 100 L bag bioreactors via a peristaltic pump on a movable cart to a 1500 L seed bioreactor. As described in the media preparation section (5.1.2), about 667 L of fresh serum free media is prepared and added to the bioreactor after passing through a sterile filter to remove possible contaminants such as bacteria. Seed bioreactor 1 has a working volume of 70% to allow for proper agitation with an installed agitator. Process control is achieved using a package provided by ABEC. The temperature is kept at 37°C over the course of 4 days with a pH of 7.0 and a DO level of 50%.

5.3.2 Seed Bioreactor 2 (SBR-102)

The cells must then be transferred from the 1500 L bioreactor, via a permanent peristaltic pump, to a 4500 L seed bioreactor for additional scale up. About 2066 L of fresh serum free media is prepared and added to the bioreactor after passing through a sterile filter to remove possible contaminants such as bacteria. Seed bioreactor 2 has a working volume of 70% to allow for proper agitation with an installed agitator. Process control is achieved using a control package provided by ABEC. The temperature is kept at 37°C over the course of 4 days with a pH of 7.0 and a DO level of 50%.

5.4 Production Bioreactor Section (BFD-04)

5.4.1 Production Bioreactor (PBR-101)

In order to obtain a 3.5 g/L titer of monoclonal antibodies in solution, the cells must be transferred to a 14,000 L fed-batch production bioreactor, via a permanent peristaltic pump, where they are allowed to continue to grow and secrete this valuable product. Serum free media and glucose will be incrementally added throughout the process in order to obtain the desired

titer level. About 2066 L of fresh serum free media is prepared and added to the bioreactor at the very start of fermentation while additional amounts will be added over the course of 12 days. The production bioreactor has a working volume of 70% to allow for proper agitation with an installed agitator. Process control is achieved using a control package provided by ABEC, and the temperature will be maintained at 37°C with a set point pH of 7.0. Two production bioreactors of equal size are staggered in order to provide a greater capacity and output of monoclonal antibodies that also reduces the amount of idle cycle time. See the scheduling section for more information.

5.5 Primary Recovery Section (BFD-05)

5.5.1 Harvest Tank (P-26/V-201)

After the harvest tank is initially sterilized with SIP operations, the contents of the production bioreactor are transferred to this unit through a peristaltic pump. The tank is maintained at 1-2 psig and 25°C. The pH of the harvest tanks is adjusted to 7.0 with 0.1 M H₃PO₄. Once these measures have taken place, the product is ready to be purified. As a safety precaution, all wastes removed from this section of the process are collected in a biowaste tank, and sterilized by heating to 180 °C. After the product stream fully exits the harvest tank, this unit is cleaned with CIP operations.

5.5.2 Centrifugation (P-28/DS-201)

The generated biomass and other suspended components are removed using a Disc-Stack centrifuge (DS-201). The centrifuge is operated at 25°C, with a throughput of 2,000 L/h. During this step, roughly 2% of the monoclonal antibody is lost in the solids waste stream, resulting in a product yield of 98%. The supernatant containing the monoclonal antibody then passes through a 0.2 µm sterile filter before entering a centrifugation pool tank (P-32/V-202) to await further

processing. The centrifuge and centrifugation holding tank are sterilized through SIP and CIP operations. The sterile filtration membranes are disposed of after each batch.

5.6 Pepsin Cleavage (BFD-06a)

5.6.1 Diafiltration (P-35/DF-201)

Following centrifugation, the product-containing stream is split and passes through two diafiltration units to concentrate the stream from 3.56 g/L to 10.36 g/L of mAb, thus preparing it for pepsin cleavage. Filters are used with a pore size which correlates to a molecular weight cutoff (MWCO) of 30 kDa so that 150 kDa mAbs are retained. The diafiltration unit is maintained at 25°C, and has a pressure change of 43.5 psig associated with it. This diafiltration system, including reusable membranes, is sterilized through SIP and CIP operations after each batch.

5.6.2 Pepsin Cleavage (P-36/R-201)

Upon entering the cleavage reactor, the concentrated monoclonal antibody stream is mixed with an equal amount of digestion buffer (made up of 20 mM sodium acetate and pH adjusted to 4.5 using hydrogen chloride). Pepsin (immobilized on 6% cross-linked beaded agarose) is then transferred into the reactor, and the reaction vessel is heated to 37°C. The reactor is maintained at this temperature with constant agitation for 5 hours. The cleavage reaction produces one F(ab')₂ fragment and one Fc fragment from each individual antibody (see figure 2.3). The reaction vessel is sterilized with SIP and CIP operations.

5.6.3 Plate and Frame Filtration (P-38/PFF-201)

Following the cleavage reaction, the immobilized pepsin is removed from the product stream through plate and frame (P&F) filtration. The plate and frame filtration system operates at 25°C and has a total filter area of 23.23 m². Following the initial filtration, the filter cake is washed with 2322.94 L of 10 mM Tris-HCl, pH 7.5 for maximum product recovery. The pepsin

removed from this filtration can be washed and reused for additional cleavage reactions, but for the purposes of this analysis this has not been model. The enclosed P&F filtration unit is sterilized with SIP and CIP procedures.

5.6.4 Diafiltration (P-42/DF-202)

Following P&F filtration, the product stream passes through another diafiltration unit. This diafiltration step is used to exchange the buffer of this stream to that necessary for the disulfide reduction reaction and concentrate the $F(ab')_2$ from 4.6 mg/mL to 10 mg/mL. The reduction protocol indicates that any similar buffer to that given with a concentration of EDTA between 1-10 mM is acceptable for this reaction, so the same buffer is used as that given in the protocol and used later in the process for the PEGylation reaction. This reduction buffer is made up of 2.0 mM EDTA and 0.1 M sodium phosphate at a pH of 6.0. Filters are used with a MWCO of 30 kDa so that 100 kDa $F(ab')_2$ fragments are retained, while some of the very small degraded Fc fragments (< 50 kDa) created during the cleavage reaction are filtered out. The diafiltration unit is maintained at 25°C, and has a pressure change of 43.5 psig associated with it. Cleaning is performed before and after every batch using CIP and SIP procedures.

5.6.5 Disulfide Reduction (P-44/R-202)

Once the $F(ab')_2$ fragments are produced in the cleavage reaction and transferred to reduction buffer in the diafiltration step, they are ready to go into the disulfide reduction reactor. The hinge region disulfide bonds are broken by the mild reducing agent 2-Mercaptoethylamine·HCl (2-MEA), which will only reduce these bonds unlike stronger thiols which may also reduce the disulfide bonds between the heavy and light chains of the Fab' fragments (Humphreys *et al.*, 2007). This reaction then gives two 50 kDa Fab fragments from each $F(ab')_2$ molecule, each of which retains a portion of the hinge region, including a cysteine (See Figure 2.4). This cysteine contains a thiol group which can then be specifically PEGylated later in the process (Humphreys *et al.*, 2007). 2-MEA at a concentration of 50 mM is reacted

with the F(ab')₂ stream in reduction buffer at 37°C for 90 minutes in order for this reaction to occur. The reactor is then returned to room temperature (25°C). Validated cleaning is performed before and after every batch using CIP and SIP procedures.

5.6.7 Diafiltration (P-47/DF-203)

After the reduction reaction goes to completion, the product stream is split and passes through another diafiltration unit. This diafiltration step is used to exchange the reduction buffer with WFI so that the Fab' fragments can go into the Protein-A chromatography column, while maintaining the same Fab' concentration of 10 mg/ml. Filters are used with a MWCO of 10 kDa so that 50 kDa Fab' fragments are retained, while any remaining 2-MEA (114 Da) from the reduction reaction are filtered out. The diafiltration unit is maintained at 25°C, and has a pressure change of 14.5 psig associated with it. Cleaning is performed before and after every batch using CIP and SIP procedures.

5.7 Protein A Chromatography (BFD-07)

5.7.1 Protein A Chromatography (P-49/C-201)

This chromatography step is used to purify the monoclonal antibody Fab' fragments and remove the bulk of contaminant (unwanted) proteins in the production stream. The Fc fragments produced during the cleavage reaction bind to this affinity chromatography column, and can thus be separated from the Fab' products. Before loading the product stream onto the column, the column and skid undergo some preparatory steps. First, the system is drained to remove the storage solution (regeneration buffer). The skid and column are cleaned by flushing with WFI, and then equilibrated by flushing with equilibration buffer. All wastes are drained into the neutralization waste tank.

The product stream is then loaded into the column with a linear velocity of 200 cm/h. The resin in use, nProtein A sepharose, has a binding capacity of 50 g/l. After loading, the column is

washed with Wash Buffer. The column is then eluted isocratically with an eluant volume five packed bed volumes. The yield for the mAb Fab' fragments for this step is 90%.

The column is regenerated with regeneration buffer, and then cleaned in place using a separate chromatographic rig CIP, which involves a wash with 0.1M NaOH, followed by a wash with WFI.

5.8 Chemical Virus Inactivation (BFD-08)

5.8.1 Diafiltration (P-54/DF-204)

The protein solution then passes through a sterile filtration unit to a diafiltration system. The stream is concentrated 5X and diafiltered 2X. The yield on product is 97%, as a small percentage is denatured in the process. This diafiltration step removes salts, solvents and other unwanted components from the solution, resulting in a higher concentration of cleaved monoclonal antibody. Filters are used with a MWCO of 10 kDa so that 50 kDa Fab' fragments are retained. This diafiltration is operated at 25°C. The diafiltration system is cleaned with SIP and CIP procedures.

5.8.2 Chemical Virus Inactivation (P-56/V-207)

The concentrated protein solution is chemically treated for 1.5 hours with polysorbate 80 to inactivate enveloped viruses. Polysorbate 80 (also known as Tween 80) is an extremely mild and effective oil-in-water emulsifier and solubilizer. This chemical disrupts the interactions between molecules in the lipid coat of viruses, rendering the coat dysfunctional and impeding replication. This process operates at 25°C. The chemical virus inactivation tank is later cleaned with SIP and CIP procedures.

5.9 Ion Exchange Chromatography (BFD-09/BFD-10)

Ion exchange chromatography makes use of the charge properties of molecules to separate them. By changing both the ionic concentration and the pH of a solution, the charge of a

molecule can be manipulated, allowing it to bind to opposite charged resins that are packed in a column.

5.9.1 Cation Exchange Chromatography (P-68/C-301)

Cation exchange chromatography is used to bind positively charged molecules to its negatively charged resins. The Fab is positively charged under acidic conditions, such as Cation Buffer A (pH 5.5), and binds to the cation exchange resin, Toyopearl Gigacap S-650M. The column is manufactured by GE-Healthcare and is a Chromaflow 1000 column. The column is 1.0 m in diameter, 0.50 m tall, and has a bed height of 0.137 m and a column volume of 392.7 L. The distributor is made of polypropylene; the seals are made of FEP-encapsulated silicone; and the remaining parts are made of 316L stainless steel.

After loading the column with the resin, the column is equilibrated with five column volumes of Cation Buffer A using the Cat-Equil stream from tank V-301. Cation Buffer A contains MES (2-(N-morpholino)ethanesulfonic acid) at a pH of 5.5. MES was chosen instead of the more common acetate buffers because acetate buffers need to be used at a pH of 4.5, which can lead to insolubility, denaturation, and loss of activity of the Fab. The incoming solution containing the Fab will first be mixed online in a 1:9 ratio with Cation Buffer A and loaded into the column. At lower pH, the monoclonal antibody fragment has a positive net charge, allowing it to bind to the negatively charged resin. Because only the monoclonal antibody fragments bind, other impurities, such as host cell proteins and any leached Protein A particles flow through to a waste stream (Waste-15). The beads are then washed with 5 column volumes of Cation Buffer A using the Cat-Wash stream to remove any extra waste still in the resin. The Fab fragments are then eluted in a gradient with 15 column volumes of Cation Buffer B (stream Cat-Elute from tank V-302, diluted with Cat-WFI), which contains sodium chloride, a salt that disrupts the ionic binding between the resin and the fragments. Complete stripping and regeneration of the column is then performed with 5 column volumes of Cation Buffer B to completely remove all

substances bound to the column, allowing it to be reused. Clean-In-Place is then performed using a separate chromatographic rig, which involves a wash with 0.1M NaOH, followed by a wash with WFI.

5.9.2 Anion Exchange Chromatography (P-71/C-302)

Anion exchange chromatography is then used to bind negatively-charged molecules to its positively charged resin (Toyopearl SuperQ-650M). The column is run in flow-through mode, meaning the monoclonal antibody fragments will not bind, but will instead flow through the column due to its positive charge. The molecules that do bind to the column are negatively-charged and include DNA, retrovirus, and endotoxins, all of which are extremely undesirable molecules. The column is manufactured by GE-Healthcare and is a Chromaflow 600 column. It is 0.6 m in diameter, 0.5 m tall, with a bed height of 0.205 m. It is a smaller version of the cation exchange column, and is made of the same materials: 316L stainless steel body, polypropylene distributor, and silicone seals.

With the resin already loaded into the chromatography column, the column is then equilibrated with 5 column volumes of Anion Buffer A fed from stream Anion-Equil from tank V-304. Anion Buffer A, which contains Tris and NaCl at a pH of 7.5, changes the conductivity of the monoclonal antibody solution to ensure the proper conditions for flow-through. Stream S-302 will first be mixed in tank V-303 with Anion Buffer A from stream Anion-Load and then loaded into anion exchange column C-302. The column binds any negatively charged particles, such as DNA, endotoxin, and retrovirus. The flow-through contains the monoclonal antibody fragment and is collected in storage tank V-306. The beads are then eluted with 2 column volumes of Anion Buffer A to ensure no product is retained in the resin. The column is then stripped and regenerated with 8 column volumes of Anion Buffer B, which contains a higher concentration of sodium chloride than Anion Buffer A and is used to disrupt the ionic interactions between the resin and any bound particles. The waste from stripping and

regeneration is output through Waste-16. CIP procedures are then performed using a separate chromatographic rig, which involves a wash with 0.1M NaOH, followed by a wash with WFI.

5.10 PEGylation: Thiol Reduction (BFD-11)

5.10.1 Diafiltration (P-81/DF-401)

Following the ion exchange chromatography steps, the product stream is split and passes through another diafiltration unit. This diafiltration step is used to exchange the buffer of this stream to the buffer that is necessary for the disulfide reduction reaction. In addition, this diafiltration process will concentrate the Fab' fragments from 3.9 mg/ml to 10 mg/ml. The reduction protocol indicates that any similar buffer to that given, with a concentration of EDTA between 1-10mM, is acceptable for this reaction. Therefore, the same buffer is used for this reaction as that which is utilized for the PEGylation reaction (Humphreys 2007). This reduction buffer is made up of 2.0 mM EDTA and 0.1 M Sodium Phosphate, pH 6.0. Filters are used with a MWCO of 30 kDa so that 50 kDa Fab' fragments are retained. The diafiltration unit is maintained at 25°C, and has a pressure change of 14.5 psig associated with it. Cleaning is performed before and after every batch using CIP and SIP procedures.

5.10.2 Thiol Reduction (P-83/R-401)

Now that the Fab' fragments are purified using chromatography, any thiols that may have become attached to the available cysteine during these steps must be reduced. 2-Mercaptoethylamine·HCl (2-MEA) can also be used for this purpose (Carter *et al.*, 1992). Cysteine contains a thiol group which can then be specifically PEGylated later in the process (Humphreys *et al.*, 2007). 2-MEA at a concentration of 50 mM is reacted with the F(ab')₂ stream in reduction buffer at 37°C for 90 minutes in order for this reaction to occur. The reactor is then returned to 25°C. Validated cleaning is performed before and after every batch using CIP and SIP procedures.

5.11 PEGylation Reaction (BFD-12)

5.11.1 Diafiltration (P-86/DF-402)

After the reduction reaction goes to completion, the product stream is split and passes through another diafiltration unit. This diafiltration step is used to remove any remaining 2-MEA (114 Da) from the reduction reaction while maintaining the same Fab' concentration of 10 mg/ml in PEGylation reaction buffer (which is the same as reduction reaction buffer). Filters are used with a MWCO of 10 kDa so that 50 kDa Fab' fragments are retained. The diafiltration unit is maintained at 25°C, and has a pressure change of 14.5 psig associated with it. Cleaning is performed before and after every batch using CIP and SIP procedures.

5.11.2 PEGylation Reaction (P-88 / R-402)

Once any thiols attached to the Fab' fragments are reduced, the molecules are ready to go into the PEGylation reactor. The hinge region cysteine that remains on the 50 kDa Fab' fragments after pepsin cleavage and disulfide reduction is available to be specifically PEGylated with a 40 kDa thiol-reactive PEG molecule. The reaction occurs in PEGylation buffer containing the Fab' fragments and a 1:2 molar excess of PEG at 25°C for 2 hours. Validated cleaning is performed before and after every batch using CIP and SIP procedures.

5.11.3 Diafiltration (P-91/DF-403)

After the PEGylation reaction goes to completion, the product stream is split and passes through another diafiltration unit. This diafiltration step is used maintain the same Fab' concentration of 10 mg/ml, but switch buffers from PEGylation reaction buffer to WFI. Filters are used with a MWCO of 30 kDa so that 90 kDa PEGylated Fab' products are retained. The diafiltration unit is maintained at 25°C, and has a pressure change of 14.5 psig associated with it. Cleaning is performed before and after every batch using CIP and SIP procedures.

5.12 Cation Exchange Chromatography (BFD-13)

5.12.1 Cation Exchange Chromatography Column (P-101/C-401)

This cation exchange chromatography column contains a negatively charged, biopharmaceutical-grade MacroCap SP resin which specifically binds PEGylated proteins, which are positive under acidic conditions. This resin exploits the fact that PEG molecules are neutral, meaning that the mono-PEGylated proteins will have a lower charge than any unreacted (non-PEGylated) Fab' fragments while having a higher charge than the excess PEG molecules. This column will be used to separate the PEGylated Fab' fragments with a very high specificity, resulting in 99% recovery of the desired protein product.

The resin consists of a matrix made of a cross-linked copolymer of allyl dextran and N,N-methylene bisacrylamide, which has a binding capacity of 150 mg/ml and a total ionic capacity of 0.10 to 0.13 mmol H⁺/ml medium. The matrix is very porous, so there is a large amount of surface area for the large protein product to bind. The resin will be packed in a bed of volume 154.46 L in a Chromaflow 1000 Stainless Steel 316L column of volume 617.85 L total. The linear velocity in the column is 120 cm/h. Cation Buffer 1 is used for equilibration, loading, and washing and consists of 0.2 M phosphate in WFI. Cation Buffer 2 is used for elution and stripping and consists of 0.02 M phosphate (pH 6.8) and 1 M NaCl in WFI.

After the resin bed is packed in the column, it is equilibrated with Cation Buffer 1 from the holding tank where this buffer is prepared and stored. Before loading the PEG-Fab' stream into the column, this stream is mixed with acidic Cation Buffer 1, in which Fab' fragments will exhibit positive charge. The beads are washed with Cation Buffer 1 to remove any waste or unbound particles still in the resin. The PEG-Fab' fragments (and non-PEGylated Fab' fragments) are eluted in a gradient with 20 column volumes of Cation Buffer 2, which contains sodium chloride, a salt that disrupts the ionic binding between the resin and the fragments. Since

PEG-Fab' fragments are less positively charged than PEG molecules, but more positively charged than non-PEGylated proteins, the desired protein will elute in between the PEG and Fabs. This is why a gradient must be used to collect the desired product, after it is experimentally determined which column volumes the PEG-Fab' will elute into. Once the product is recovered, the column is stripped and regenerated with Cation Buffer 2 to completely remove anything still bound to the resin. Once this is validated, the column and resin can be reused for the next batch. Finally, the column is Cleaned-In-Place using a chromatographic rig that will wash the equipment with 0.1M NaOH and then rinse it with WFI.

5.13 Final Filtration and Packaging (BFD-14)

5.13.1 Diafiltration (P-104/DF-501)

Diafiltration is a process used to filter out different substances by molecular weight, while exchanging buffers. In this case, the reagents and impurities from previous downstream purification processes such as PEGylation and Ion Exchange Chromatography will be filtered out, leaving the PEGylated monoclonal antibody fragment in its final buffer. Using filters with a 30 kDa MWCO, purified water flushes small ions and molecules through the membrane, leaving the larger PEGylated antibody fragment (90 kDa). The cassette is then diafiltered with phosphate buffered saline (PBS). PBS is a buffer solution and its ion and osmolarity concentrations match those of the human body and helps maintain a constant pH. Therefore, it is the most ideal final buffer solution for any injectable therapeutic. This process is also called a buffer exchange, as the previous solution is removed and replaced with PBS.

5.13.2 Viral Exclusion Filtration (P-106/DE-501, P-107/DE-502)

While ion exchange chromatography removes some virus particles, a final viral filtration step is still necessary to eliminate any possible virus particles from being packaged with the monoclonal antibody fragment. Viral filtration is necessary because the mammalian cell line that

is used to produce monoclonal antibodies may contain endogenous viruses that may be harmful to humans. Also, because viruses are extremely small and can survive for long periods without a host, they may also enter the system through raw materials or feed streams. For this reason, viral filtration is performed at the end of the process to ensure that all viruses are cleared from the system.

Filtration of viruses is split into two steps: retrovirus filtration and parvovirus filtration. Retrovirus filters are capable of removing retroviruses that are generally about 50 nm or larger. Parvoviruses, which are about 20 nm, need to be filtered out using filters that are much more size-selective. Since the PEGylated monoclonal antibody fragment is about 10 nm, both of these filters will allow the desired product to pass through.

Both retrovirus filtration systems and parvovirus filtration systems consist of normal-flow filters that remove the potentially harmful viruses from the product stream. Normal-flow filtration, or dead-end filtration, is a filtration mode where the fluid runs perpendicular to the filter membrane, trapping the virus in the filter while allowing the target protein to pass through. These filters are manufactured by Millipore and are contained within filter housings. A removal of a log of virus means that the viral load of the stream will be reduced by a factor of 10. The Millipore Viresolve filters remove over 6 logs of retrovirus (or a reduction factor of one million) and over 4 logs of parvovirus (a reduction factor of ten thousand), while allowing for greater than 98% yield of protein. The filters themselves are disposed of and replaced after each batch to ensure sterility.

5.13.3 Packaging/Freezing (P-108/DCS-101)

The purified PEGylated monoclonal antibody fragment contained in PBS will need to be transported to another company for formulation. However, proteins can denature, become unstable or inactive if they are allowed to sit at room temperature. The easiest way to ensure the

long term stability of the product is to freeze them down to very cold temperatures (anywhere between -20°C to -85°C).

The product is dispensed into 50 L sterile plastic bags for storage. This is done by the SciLog Fillmaster system, which is a pump and valve system that allows for accurate distribution of the product. The bags are made of HyQ CX5-14 film, which are sterile, disposable bags manufactured by HyClone that can protect the product in ultra low temperatures. The filled bags are then frozen in an ultra cold freezer that can operate at temperatures down to -85°C. This will ensure long-term stability and prevent denaturation or damage to the product. The frozen product will be sent to another facility where it will be lyophilized and bottled for increased shelf life and patient delivery.

6.0 Plant Utility Requirements

The major utility needs of the plant consist of electricity, process water, and steam.

Electricity is the most expensive of the three and costs approximately \$98,000 a year. These calculations are based off a \$0.08 per kWh rate obtained from NSTAR, a Massachusetts energy provider. Operation of process machinery costs roughly \$5300 a year, with much of the energy consumed by the production bioreactors. The additional equipment actually consumes most of the energy in the plant. The HVAC system uses 71% of the electricity in the plant, while the WFI still and clean steam generator are the other significant consumers. The table shown in section 6.1 displays the electricity requirements and related costs.

Process water is the other major utility that will be used to produce monoclonal antibodies. The plant will require approximately 2.7 million liters of process water a year. This water will also be used to generate WFI and steam for buffers and SIP. At a rate of \$0.543 per 1000 liters, a rate obtained from the Aquarion Water Company of Massachusetts, the cost of the process water will be approximately \$1470 a year. The cost greatly increases when purifying to WFI using WFI stills. This cost is accounted for in the electricity costs.

6.1 Electricity Requirements for Equipment

Electricity Costs	Unit Cost (\$/kWh)	Amount (kWh/batch)	Cost (\$/batch)	Cost/Year (\$)
Upstream				
P-1	0.08	0.08	\$0.01	\$0.35
P-3	0.08	1.37	\$0.11	\$6.03
P-4	0.08	6.2	\$0.50	\$27.28
P-6	0.08	0.03	\$0.00	\$0.13
P-8	0.08	0.03	\$0.00	\$0.13
P-9	0.08	28.54	\$2.28	\$125.58
P-10	0.08	0.07	\$0.01	\$0.31
P-12	0.08	0.08	\$0.01	\$0.35
P-14	0.08	0.08	\$0.01	\$0.35
P-15	0.08	88.52	\$7.08	\$389.49
P-16	0.08	0.12	\$0.01	\$0.53
P-18	0.08	0.21	\$0.02	\$0.92
P-20	0.08	0.21	\$0.02	\$0.92
P-22	0.08	0.04	\$0.00	\$0.18
P-24	0.08	0.04	\$0.00	\$0.18
P-25	0.08	620.11	\$49.61	\$2,728.48
Total	0.08	745.73	59.6584	3281.212
Primary Recovery/Pepsin				
P-27	0.08	0.67	\$0.05	\$2.95
P-28	0.08	143.8	\$11.50	\$632.72
P-29	0.08	0.6	\$0.05	\$2.64
P-31	0.08	0.6	\$0.05	\$2.64
P-33	0.08	0.6	\$0.05	\$2.64
P-35	0.08	92.78	\$7.42	\$408.23
P-36	0.08	0.79	\$0.06	\$3.48
P-38	0.08	3.97	\$0.32	\$17.47
P-40	0.08	1.15	\$0.09	\$5.06
P-42	0.08	33.7	\$2.70	\$148.28
P-43	0.08	1.16	\$0.09	\$5.10
P-45	0.08	0.17	\$0.01	\$0.75
P-47	0.08	34.17	\$2.73	\$150.35
P-48	0.08	0.59	\$0.05	\$2.60
P-50	0.08	0.59	\$0.05	\$2.60
P-52	0.08	0.59	\$0.05	\$2.60
P-54	0.08	20.72	\$1.66	\$91.17
P-55	0.08	0.12	\$0.01	\$0.53
P-57	0.08	0.12	\$0.01	\$0.53
Total	0.08	336.89	26.9512	1482.316
IEX Chromatography				
P-61	0.08	0.01	\$0.00	\$0.04
P-62	0.08	0.1	\$0.01	\$0.44
P-63	0.08	0.02	\$0.00	\$0.09
P-64	0.08	0.02	\$0.00	\$0.09
P-65	0.08	0.02	\$0.00	\$0.09
P-66	0.08	0.02	\$0.00	\$0.09
P-70	0.08	0.15	\$0.01	\$0.66
P-73	0.08	0.14	\$0.01	\$0.62
P-74	0.08	0.01	\$0.00	\$0.04
P-75	0.08	0.01	\$0.00	\$0.04
P-76	0.08	0.02	\$0.00	\$0.09

P-79	0.08	0.04	\$0.00	\$0.18
Total	0.08	0.56	0.0448	2.464
PEGylation				
P-81	0.08	39.93	\$3.19	\$175.69
P-82	0.08	0.06	\$0.00	\$0.26
P-84	0.08	0.06	\$0.00	\$0.26
P-86	0.08	11.94	\$0.96	\$52.54
P-87	0.08	0.06	\$0.00	\$0.26
P-89	0.08	0.03	\$0.00	\$0.13
P-91	0.08	6.78	\$0.54	\$29.83
P-94	0.08	0.03	\$0.00	\$0.13
P-95	0.08	0.08	\$0.01	\$0.35
P-96	0.08	0.03	\$0.00	\$0.13
P-97	0.08	0.04	\$0.00	\$0.18
P-98	0.08	0.03	\$0.00	\$0.13
P-99	0.08	0.03	\$0.00	\$0.13
Total	0.08	59.1	4.728	260.04
Final Filtration				
P-104	0.08	2.00	\$0.16	\$8.80
P-102	0.08	0.02	\$0.00	\$0.09
P-105	0.08	0.04	\$0.00	\$0.18
P-109	0.08	44.00	\$3.52	\$193.60
P-108	0.08	0.03	\$0.00	\$0.13
Total	0.08	46.09	3.69	202.80
Process Equipment Total		1188.37	95.07	5228.83
Incubators	0.08	49.92	3.9936	\$219.65
HVAC	0.08	15927.3	1274.184	\$70,080.12
Steam Generator	0.08	938.48	\$75.08	\$4,129.30
CIP Skids	0.08	87.84	\$7.03	\$386.50
Water Treatment Package	0.08	734.09	\$58.73	\$3,230.00
WFI Still	0.08	2,391.59	\$191.33	\$10,523.00
Biowaste Inactivation	0.08	233.30	\$18.66	\$1,026.53
Waste Neutralization	0.08	911.90	\$72.95	\$4,012.35
Additional Equipment Total		21274.42	1701.954	\$93,607.45
Grand Total		22462.79	1797.02	\$98,836.28

7.0 Major Unit Descriptions

7.1 Inoculum Prep Section (BFD-01)

7.1.1 T-Flasks (P-1/TFR-101)

The T-flasks used for initial inoculation are purchased from Nunc International for the cost of \$205.01 for a case of 30 flasks. These flasks are non-treated and are provided in sterile condition so that the cells will not be contaminated in any way when they come into contact with the surface of the flask. The flasks are made of polystyrene with a filter cap and can hold up to 225 mL of volume, but the suggested working volume is 70-100 mL. The T-flasks are easily disposed of after use. Twenty T-flasks will be utilized per batch. The flasks will be manipulated in a Bio hood.

7.1.2 Roller Bottles (P-2/RBR-101)

The roller bottles used for the second step of the seed train are also purchased from Nunc International. The cost for a case of 22 bottles is \$426.75. These roller bottles, like the T-flasks, are non-treated and are provided in sterile condition. The bottles are made of Polyethylene terephthalate (PETG) and have a culture area of 1800 cm² with a suggested working volume of 200-1000 ml. Eleven roller bottles will be used per batch.

7.1.3 Bag Bioreactor 1 (P-3/BBS-101)

The pre-sterilized disposable bioreactor chamber is equipped with ports for sterile aeration, seeding, harvesting, sampling and analysis. The rocker unit is used to control and monitor temperature, aeration rate, and rocking speed to obtain proper cell growth. Each bag bioreactor unit for this stage of the process is able to hold one 20 L bag. The unit is purchased from Sartorius Stedim Biotech for \$33,000. This, however, is based on a quote from Applikon who produces a similar product. The name of the model is the BIOSTAT® CultiBag RM Rocker

20/50 Optical Package. Disposable bags with sensors and ports for oxygen, media, and buffer flow are also purchased from Sartorius and retail for \$447 per bag.

7.1.4 Bag Bioreactor 2 (P-4/BBS-101)

The second set of bag bioreactors has the same functions as the first set which were described in the previous section. Each bag bioreactor unit for this stage of the process is able to hold one 100 L bag. The unit is purchased from Sartorius Stedim Biotech for \$39,000. This, however, is based on a quote from Applikon who produces a similar product. The name of the model is the BIOSTAT® CultiBag RM Rocker 200 Optical Package. Disposable bags with sensors and ports for oxygen, media, and buffer flow are also purchased from Sartorius and retail for \$447 per bag.

7.1.5 Storage/Mixing Tank (P-5/MP-101)

This tank is used to store and mix powdered serum free media before it is fed through a sterile filter and into the first seed bioreactor. The tank is made from stainless steel 316, has a volume of 1000 L, and has a working capacity of 70%. It stands 2.2 m tall and is 0.8 m in diameter. For sterilization, CIP and SIP are used after each batch. The tank operates at room temperature and at 1 bar. The tank is fabricated by Sharpsville Container and costs \$117,000.

7.1.6 Pump (P-6/PM-101)

This pump is used to transfer fluid from the first media prep storage tank to the first sterile filter of the process. This is a very low powered 1 kW (1.34 hp) peristaltic pump. It operates at room temperature with an approximate pressure drop of 25 psi. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.1.7 Sterilization Filter (P-7/DE-101)

This 0.2 µm filter is used to remove bacteria and other impurities from the serum free media prior to feeding the first seed bioreactor. It is approximately 30 inches in size with a

filtration area of 1.8 m². The filter operates at room temperature with a differential pressure of 0.5 bar. The filters require a type of housing for security that requires a one time purchase from Sartorius Stedim Biotech for the cost of \$1908. The filters are disposable, and therefore need to be replaced after every batch. These filters are also purchased from Sartorius under the model name Sartopore 2 for the cost of \$608 per unit.

7.2 Seed Bioreactor Section (BFD-02/BFD-03)

7.2.1 Pump (P-8/PM-102)

This pump is used to transfer fluid from the first sterilization filter to the first seed bioreactor. This pump is exactly the same as (PM-101) described previously. This is a very low powered 1 kW (1.34 hp) peristaltic pump. It operates at room temperature with an approximate pressure drop of 25 psi. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.2.2 Seed Bioreactor 1 (P-9/SBR-101)

This is a 1500 L jacketed seed bioreactor with agitator and control package used for continued cell growth and production of monoclonal antibodies. The bioreactor is purchased from ABEC. The bioreactor is 2.3 m tall and 0.9 m in diameter. It has a working capacity of 70% and CIP and SIP are necessary for validated cleaning following each batch. The bioreactor operates at 37°C and 1 bar over the course of 4 days. This temperature is maintained by filling the water jacket with water at 37°C at an average flow rate of approximately 0.04 kg/s. This bioreactor also comes with an add-on control system that provides automated control of environmental conditions and feed scheduling. The purchase cost from ABEC for this bioreactor is \$495,000.

7.2.3 Pump (P-10/PM-103)

This pump is used to transfer fluid from the first seed bioreactor to the second seed bioreactor. This pump is similar to both PM-101 and PM-102 which were described previously. This is a very low powered 1 kW (1.34 hp) peristaltic pump. It operates at room temperature with an approximate pressure drop of 25 psi. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.2.4 Storage/Mixing Tank (P-11/MP-102)

This tank is used to store and mix powdered serum free media before it is fed through a sterile filter and into the second seed bioreactor. The tank is made from stainless steel 316, has a volume of 3000 L, and has a working capacity of 70%. It stands 3.3 m tall and is 1.1 m in diameter. For sterilization, CIP and SIP are used after each batch. The tank operates at room temperature and at 1 bar. The tank is fabricated by Sharpsville Container and has a purchase cost of \$120,000.

7.2.5 Pump (P-12/PM-104)

This pump is used to transfer fluid from the second media prep storage tank to the second sterile filter of the process. Like the others described previously, it is a very low powered 1 kW (1.34 hp) peristaltic pump. It operates at room temperature with an approximate pressure drop of 25 psi. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.2.6 Sterilization Filter (P-13/DE-102)

This 0.2 μm filter is used to remove bacteria and other impurities from the serum free media prior to feeding the second seed bioreactor. It is approximately 30 inches in size with a filtration area of 1.8 m^2 . The filter operates at room temperature with a differential pressure of 0.5 bar. The filters require a type of housing for security that requires a one-time purchase from

Sartorius Stedim Biotech for the cost of \$1908. The filters are disposable, and therefore need to be replaced after every batch. These filters are also purchased from Sartorius under the model name Sartopore 2 for the cost of \$608 per unit.

7.2.7 Pump (P-14/PM-105)

This pump is used to transfer fluid from the second sterilization filter to the second seed bioreactor. This pump is exactly the same as (PM-104) described previously. This is a very low powered 1 kW (1.34 hp) peristaltic pump. It operates at room temperature with an approximate pressure drop of 25 psi. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.2.8 Seed Bioreactor 2 (P-15/SBR-102)

This is a 4500 L jacketed seed bioreactor with agitator and control package. The bioreactor package is fabricated by ABEC. The bioreactor is 3.3 m tall and 1.3 m in diameter. It has a working capacity of 70% and CIP and SIP are necessary for validated cleaning following each batch. The bioreactor operates at 37°C and 1 bar over the course of 4 days. This temperature is maintained by filling the water jacket with water at 37°C at an average flow rate of approximately 0.08 kg/s. This bioreactor also comes with an add-on control system that provides automated control of environmental conditions and feed scheduling. The purchase cost from ABEC for this bioreactor is \$585,000.

7.2.9 Pump (P-16/PM-106)

This pump is used to transfer fluid from the second seed bioreactor to the production bioreactor. This pump is similar to both PM-104 and PM-105 which were described previously. This is a very low powered 1 kW (1.34 hp) peristaltic pump. It operates at room temperature with an approximate pressure drop of 25 psi. The pump is sterilized via CIP and SIP after every

batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.2.10 Storage/Mixing Tank (P-17/MP-103)

This tank is used to store and mix powdered serum free media before it is fed through a sterile filter and into the production bioreactor. The tank is made from stainless steel 316, has a volume of 7700 L, and has a working capacity of 70%. It stands 4.5 m tall and is 1.5 m in diameter. For sterilization, CIP and SIP are used after each batch. The tank operates at room temperature and at 1 bar. The tank is fabricated by Sharpsville Container and has a purchase cost of \$130,000.

7.2.11 Pump (P-18/PM-107)

This pump is used to transfer fluid from the third media prep storage tank to the third sterile filter of the process. Like the others described previously, it is a very low powered 1 kW (1.34 hp) peristaltic pump. It operates at room temperature with an approximate pressure drop of 25 psi. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.2.12 Sterilization Filter (P-19/DE-103)

This 0.2 μm filter is used to remove bacteria and other impurities from the serum free media prior to feeding the production bioreactor. It the same as the filters that were previously described in that it is approximately 30 inches in size with a filtration area of 1.8 m^2 . The filter operates at room temperature with a differential pressure of 0.5 bar. The filters require a type of housing for security that requires a one-time purchase from Sartorius Stedim Biotech for the cost of \$1908. The filters are disposable, and therefore need to be replaced after every batch. These filters are also purchased from Sartorius under the model name Sartopore 2 for the cost of \$608 per unit.

7.2.22 Pump (P-20/PM-108)

This pump is used to transfer fluid from the third sterilization filter to the production bioreactor. This pump is exactly the same as (PM-107) described previously. This is a very low powered 1 kW (1.34 hp) peristaltic pump. It operates at room temperature with an approximate pressure drop of 25 psi. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.2.23 Storage/Mixing Tank (P-21/MP-104)

This tank is used to store and mix powdered serum free media that is used for fed batch in the production bioreactor before it is fed through another sterile filter and into the production bioreactor. The tank is made from stainless steel 316, has a volume of 1600 L, and has a working capacity of 70%. It stands 2.6 m tall and is 0.9 m in diameter. For sterilization, CIP and SIP are used after each batch. The tank operates at room temperature and at 1 bar. The tank is fabricated by Sharpsville Container and has a purchase cost of \$117,000.

7.2.24 Pump (P-22/PM-109)

This pump is used to transfer fluid from the fourth media prep storage tank to the fourth sterile filter of the process. Like the others described previously, it is a very low powered 1 kW (1.34 hp) peristaltic pump. It operates at room temperature with an approximate pressure drop of 25 psi. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.2.25 Sterilization Filter (P-23/DE-104)

This 0.2 μm filter is used to remove bacteria and other impurities from the serum free media prior to feeding the production bioreactor. It is approximately 30 inches in size with a filtration area of 1.8 m^2 . The filter operates at room temperature with a differential pressure of 0.5 bar. The filters require a type of housing for security that requires a one-time purchase from

Sartorius Stedim Biotech for the cost of \$1908. The filters are disposable, and therefore need to be replaced after every batch. These filters are also purchased from Sartorius under the model name Sartopore 2 for the cost of \$608 per unit.

7.3 Production Bioreactor Section (BFD-04)

7.3.1 Pump (P-24/PM-110)

This pump is used to transfer fluid from the first sterilization filter to the first seed bioreactor. This pump is exactly the same as (PM-109) described previously. This is a very low powered 1 kW (1.34 hp) peristaltic pump. It operates at room temperature with an approximate pressure drop of 25 psi. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.3.2 Production Bioreactor (P-25/PBR-101) X 2

There are two production bioreactors used for this process that are staggered in order to provide a greater output of monoclonal antibodies and reduce the amount of idle time that would otherwise occur if two units were not used. See the scheduling section (p. 187) for further information. Each unit is a 14000 L jacketed bioreactor with agitator. The bioreactor package is fabricated by ABEC. Each is 4.8 m tall and 2.0 m in diameter. They have a working capacity of 70%. CIP and SIP are mandatory for validated cleaning following each batch. Each operates at 37°C and 1 bar over the course of 9 days. The temperature in each bioreactor is maintained by filling the water jacket with water at 37°C at an average flow rate of approximately 0.25 kg/s. This bioreactor also comes with an add-on control system that provides automated control of environmental conditions and feed scheduling. The purchase cost from ABEC for each bioreactor is \$661,000.

7.4 Primary Recovery (BFD-05)

7.4.1 Surge Tank (P-26/V-201)

The storage tank is used to store the output of the production bioreactor prior to further processing. This unit is an 11,000 L jacketed blending tank made of 316L Stainless Steel with an electropolished finish. The unit is 5.0 m tall, has a diameter of 1.67 m and has a working capacity of 90%. It operates at 25°C and 1.103 bar. This unit is sterilized via CIP and SIP procedures following every batch. This surge tank is manufactured by Sharpsville Container, with a purchase cost of \$117,000.

7.4.2 Pump (P-27/PM-201)

This pump is used to transfer fluid from the bioreaction surge tank to the centrifugation unit. This is a very low powered 1 kW (1.34 hp) peristaltic pump. It operates at room temperature with an approximate pressure drop of 25 psi. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.4.3 Centrifuge (P-28/DS-201)

The generated biomass and other suspended compounds are removed using a Disc-Stack Centrifuge. The centrifuge in use the BTAX 215H-31 CEP produced by Alfa-Laval. This unit is constructed from 316L Stainless Steel with an electropolished finish. The maximum bowl speed of the centrifuge is 6,065 rpm, and requires a power input of 13-28 kW (depending on centrifuge speed selected). This unit operates at 25°C, with a throughput of 2,000 L/h. The centrifuge is sterilized after each batch with CIP and SIP procedures. The purchase cost of this centrifuge from Alfa-laval is \$421,000.

7.4.4 Pump (P-29/PM-202)

This pump is used to transfer fluid from the centrifugation unit to a sterile filtration unit. This, as the previously described pump, operates at a very low powered 1 kW (1.34 hp) peristaltic pump. Operation is maintained at room temperature with an approximate pressure drop of 25 psi. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.4.5 Sterilization Filter (P-30/DE-201)

This 0.2 μm filter is used to remove bacteria and other impurities from the supernatant of the centrifugation process. It is approximately 30 inches in size with a filtration area of 1.8 m^2 . The filter operates at room temperature with a differential pressure of 0.5 bar. The filters require a type of housing for security that requires a one-time purchase from Sartorius Stedim Biotech for the cost of \$1908. The filters are disposable, and therefore need to be replaced after every batch. These filters are also purchased from Sartorius under the model name Sartopore 2 for the cost of \$608 per unit.

7.4.6 Pump (P-31/PM-203)

This pump is used to transfer fluid through the sterile filtration unit to the centrifugation pool tank. This, as the other previously described pumps, operates at a very low powered 1 kW (1.34 hp) peristaltic pump. The pump is maintained at room temperature and has approximate pressure drop of 25 psi associated with it. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.4.7 Centrifugation Pool Tank (P-32/V-202)

This jacketed storage tank is used to store the supernatant of the centrifugation procedure prior to further processing. This unit is a 10,000 L blending tank made of 316L Stainless Steel

with an electropolished finish. The unit is 4.8 m tall and has a diameter of 1.6 m. The working capacity of this tank is 90%. It operates at 25°C and 1.103 bar. This unit is sterilized via CIP and SIP procedures following every batch. This surge tank is manufactured by Sharpsville Container, with a purchase cost of \$117,000.

7.5 Pepsin Cleavage (BFD-06a)

7.5.1 Pump (P-33/PM-204)

This pump is used to transfer fluid from the centrifugation pool tank to the diafiltration system. This, as the other previously described pumps, operates at a very low powered 1 kW (1.34 hp) peristaltic pump. The pump is maintained at room temperature and has approximate pressure drop of 25 psi associated with it. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.5.2 Diafiltration Storage Tank (P-34/V-203)

This jacketed storage tank is used to store the production stream during the diafiltration process. This unit is a 10,000 L blending tank made of 316L Stainless Steel with an electropolished finish. The unit is 4.8 m tall and has a diameter of 1.6 m. The working capacity of this tank is 90%. It operates at 25°C and 1.103 bar. This unit is sterilized via CIP and SIP procedures following every batch. This surge tank is manufactured by Sharpsville Container, with a purchase cost of \$117,000.

7.5.3 Diafiltration Unit (P-35/DF-201) X2

This diafiltration system is used to concentrate the monoclonal antibody containing stream to prepare it for cleavage by immobilized pepsin. The stream is split and passed through two diafiltration units to concentrate the stream from 3.56 g/L to 10.36 g/L. The diafiltration system is manufactured by Sartorius Stedim Biotechnology. This system is comprised of

stabilized cellulose based filters (Sartocube® 302 144 59 30 E-BSW), which are each 3.0 m² with a MWCO of 30 kDa. The filter housing unit to be used is the Sartocon 2 Plus. The total filter area needed for each diafiltration system is 14.901 m². These diafiltration systems operate at 25°C and are associated with a pressure drop of 43.5 psi. The diafiltration housing costs \$11,141, which each diafiltration cartridge costs \$8,374 for a 3m² filter. The filters are replaced every 30 days.

7.5.4 Pump (P-36/PM-205)

This pump is used to transfer the antibody-containing stream from the diafiltration system to the pepsin cleavage reactor. This pump operates at 9.0 kW (12.07 hp). The pump is maintained at room temperature and has approximate pressure drop of 25 psi associated with it. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.5.5 Pepsin Cleavage Bioreactor (P-37/R-201)

Cleavage of the monoclonal antibody by pepsin occurs in this bioreactor. This unit is a 9,000L jacketed bioreactor with agitator made of 316L stainless steel with an electropolish finish. This reactor package is fabricated by ABEC. The unit is 4.06 m tall and 1.62 m in diameter. The operation of the unit occurs at 37°C and 1 bar over the course of 5 hours. Agitation is provided through a backward curved impeller, and control is provided through a DCS control system. CIP and SIP are mandatory for validated cleaning following each batch. The purchase cost from ABEC for this bioreactor is \$622,000.

7.5.6 Pump (P-38/PM-206)

This pump is used to transfer the antibody-containing stream from the pepsin cleavage reactor to the plate and frame filtration system. This, as the previously described pump, operates at 9.0 kW (12.07 hp) using a peristaltic pump. The pump is maintained at room temperature and has approximate pressure drop of 25 psi associated with it. The pump is sterilized via CIP and

SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.5.7 Plate and Frame Filtration Unit (P-38/PFF-201)

The plate and frame filtration system is used to remove and wash the immobilized pepsin used in the cleavage reaction. This filter system is the MEMBRApplan® DGM (model number 800 K 100), manufactured by Pall Corporation. The system is comprised of 29 sheet filter plates, each 1000 mm x 1000 mm, stacked horizontally in a 316L stainless steel housing unit. The unit has a total filtration area of 24.4 m², and operation occurs at 25°C. The filter unit is sterilizable via SIP and CIP operations. The purchase cost of this filtration system is \$74,000.

7.6 Disulfide Reduction (BFD-06a)

7.6.1 Pump (P-40/PM-206)

This pump is used to transfer the antibody-containing stream from the pepsin cleavage reactor to the plate and frame filtration system. This, as with the two previously described pumps, operates at 9.0 kW (12.07 hp) using a peristaltic pump. The pump is maintained at room temperature and has approximate pressure drop of 25 psi associated with it. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.6.2 Diafiltration Storage Tank (P-41 / V-204)

This unit is a 4500 L jacketed storage tank with a 90% working capacity volume of 4027.01 L (height = 3.587 m, diameter = 1.196 m) to be used during the diafiltration process between P&F Filtration and the Disulfide Reduction Reaction. It is a blending tank made of electropolished 316L Stainless Steel by Sharpsville Container for a purchase cost of \$117,000. Operating conditions are 25°C and 22.038 psi. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.6.3 Diafiltration Unit (P-42 / DF-202)

This diafiltration unit will concentrate the $F(ab')_2$ fragments from 3.68 mg/ml in pepsin Digestion Buffer to 10 mg/ml in Reduction Reaction Buffer for the Disulfide Reduction Reaction. This unit consists of 15 diafiltration filters, each with a membrane area of 3.0 m^2 to fulfill the 43.185 m^2 total membrane area requirement for this diafiltration process. The unit will use Sartorius Stedim Biotechnology's Sartocube® 302 144 59 30 E-BSW stabilized cellulose based filters in a Sartocon 2 Plus filter housing unit. The cutoff molecular weight for this filter is 30 kDa in order to retain the 100 kDa $F(ab')_2$ fragments in the retentate. The housing unit costs \$11,141 and each filter costs \$8,374, so the total cost for this unit will be \$136,751. Operating conditions are 25°C with a pressure drop of 14.5 psi. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.6.4 Pump (P-43 / PM-208)

This peristaltic pump is used to transport the $F(ab')_2$ fragments concentrated in the Reduction Reaction Buffer from the Diafiltration Unit to the Disulfide Reduction Reactor. This pump operates at 0.12 kW (0.15 hp) and 186.80 L/min. Operating conditions are 25°C with a pressure drop of 50 psi. The pump is model 840 manufactured by Watson Marlow and costs \$18,135. This model has a maximum flow rate of 133.3 L/min and maximum power of 3.1 kW (4.11 hp). It is made of electropolished Stainless Steel 316L and will be used with Bioprene 40 mm tubing. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.6.5 Disulfide Reduction Reactor (P-44 / R-202)

In this bioreactor, the reduction reaction will take place to break the hinge region bonds of the $F(ab')_2$ to give 2 Fab' fragments with a retained cysteine from the hinge region per every $F(ab')_2$. This unit is an 1800 L jacketed bioreactor with a backward curved impeller for agitation and a DCS control system. It has a volume of 1589.93 L with a height of 2.330 m, a diameter of 0.932 m and a 90% working capacity. It is made of electropolished 316L Stainless Steel by

ABEC for a purchase cost of \$508,000. The reaction is run at operating conditions of 37°C for 90 minutes. Validated cleaning is performed before and after every batch using CIP and SIP procedures.

7.6.6 Pump (P-45 / PM-209)

This peristaltic pump is used to transport the Fab' fragments concentrated in the Reduction Reaction Buffer from the Disulfide Reduction Reactor to the next Diafiltration Unit. This pump operates at 0.11 kW (0.15 hp) and 46.65 L/min. Operating conditions are 25°C with a pressure drop of 14.5 psi. The pump is model 840 manufactured by Watson Marlow and costs \$18,135. This model has a maximum flow rate of 133.3 L/min and maximum power of 3.0 kW (2.2 hp). It is made of electropolished Stainless Steel 316L and will be used with Bioprene 40 mm tubing. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.6.7 Diafiltration Storage Tank (P-46 / V-205)

This unit is a 1800 L jacketed storage tank with a 90% working capacity volume of 1597.92 L (height = 2.636 m, diameter = 0.879 m) to be used during the diafiltration process between Disulfide Reduction and the next Diafiltration Unit. It is a blending tank made of electropolished 316L Stainless Steel by Sharpsville Container for a purchase cost of \$117,000. Operating conditions are 25°C and 22.038 psi. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.6.8 Diafiltration Unit (P-47 / DF-203)

This diafiltration unit will separate out the 2-MEA and any very small Fc fragments, while maintaining a concentration of Fab' of 10 mg/ml and switching buffers from the reduction reaction buffer to WFI. This unit consists of 5 diafiltration filters, each with a membrane area of 3.0 m² to fulfill the 12.415 m² total membrane area requirement for this diafiltration process. The unit will use Sartorius Stedim Biotechnology's Sartocube® 302 144 59 30 E-BSW stabilized cellulose based filters in a Sartocon 2 Plus filter housing unit. The cutoff molecular weight for

this filter is 10 kDa in order to retain the 50 kDa Fab' fragments in the retentate. The housing unit costs \$11,141 and each filter costs \$8,374, so the total cost for this unit will be \$53,011.

Operating conditions are 25°C with a pressure drop of 14.5 psi. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.7 Protein A Chromatography (BFD-07)

7.7.1 Pump (P-48 / PM-210)

This peristaltic pump is used to transport the Fab' fragments concentrated in WFI from the Diafiltration Unit to the Protein-A Chromatography. This pump operates at 0.21 kW (0.28 hp) and 25.09 L/min. Operating conditions are 25°C with a pressure drop of 14.5 psi. The pump is model 825 manufactured by Watson Marlow and costs \$12,350. This model has a maximum flow rate of 33.3 L/min and maximum power of 1.1 kW (1.6 hp). It is made of electropolished Stainless Steel 316L and will be used with Bioprene 25 mm tubing. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.7.2 Protein A Chromatography Column (P-49/C-201)

The Protein A affinity chromatography column is used to further purify the mainstream fluid, removing the Fc fragments. The chromatography column in use is a Chromaflow® column made by GE Healthcare Life Sciences (formerly Amersham Biosciences). This system consists of a column tube, column lid, distributor, bed support, Chromaflow nozzle, seals and a stand. The distributor is made of polypropylene, the seals are made of fluoride ethylene propylene (FEP) encapsulated silicone, and the remaining parts are all made of 316L stainless steel. The column is packed with nProtein A sepharose 4 Fast Flow resin, also distributed by GE Healthcare Life Sciences. This resin has a binding capacity of 50 mg/ml and a working velocity of 30-300 cm/h. The column is operated at 25°C, at 1 bar. The cost of the column is \$190,000, and the resin is \$7,000 per liter.

7.7.3 Pump (P-50/PM-211)

This pump is used to transfer fluid from protein A chromatography column to a sterile filtration unit. This pump operates at 1 kW (1.34 hp). The pump is maintained at room temperature and has approximate pressure drop of 25 psi associated with it. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.7.4 Sterilizing Filter (P-51/DE-202)

This 0.2 μm filter is used to remove bacteria and other impurities from the clarified product stream. It is approximately 30 inches in size with a filtration area of 1.8 m^2 . The filter operates at room temperature with a differential pressure of 0.5 bar. The filters require a type of housing for security that requires a one-time purchase from Sartorius Stedim Biotech for the cost of \$1908. The filters are disposable, and therefore need to be replaced after every batch. These filters are also purchased from Sartorius under the model name Sartopore 2 for the cost of \$608 per unit.

7.8 Chemical Virus Inactivation (BFD-08)

7.8.1 Pump (P-52/PM-212)

This pump is used to transfer fluid from the sterile filtration unit to the diafiltration system. This pump operates at 1 kW (1.34 hp). The pump is maintained at room temperature and has approximate pressure drop of 25 psi associated with it. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.8.2 Diafiltration Storage Tank (P-53 / V-206)

This jacketed storage tank is used to store the production stream during the diafiltration process. This unit is a 10,000 L blending tank made of 316L Stainless Steel with an

electropolished finish. The unit is 4.8 m tall and has a diameter of 1.6 m. The working capacity of this tank is 90%. It operates at 25°C and 1.103 bar. This unit is sterilized via CIP and SIP procedures following every batch. This surge tank is manufactured by Sharpsville Container, with a purchase cost of \$117,000.

7.8.3 Diafiltration Unit (P-54/DF-204)

This diafiltration system is used to concentrate the monoclonal antibody Fab fragments 5x. The diafiltration system is manufactured by Sartorius Stedim Biotechnology. This system is comprised of stabilized cellulose based filters (Sartocube® 302 144 59 30 E-BSW), which are each 3.0 m². A 10 kDa molecular weight cutoff filter is used in order to retain the 50 kDa Fab' fragments in the retentate. The filter housing unit to be used is the Sartocon 2 Plus. The total filter area needed for each diafiltration system is 22.23 m². These diafiltration systems operate at 25°C and are associated with a pressure drop of 43.5 psi. The diafiltration housing costs \$11,141, which each diafiltration cartridge costs \$8374 for a 3m² filter.

7.8.4 Pump (P-55/PM-213)

This pump is used to transfer fluid from the sterile filtration unit to the diafiltration system. This pump, as with previous pumps, operates at 1 kW (1.34 hp). The pump is maintained at room temperature and has approximate pressure drop of 25 psi associated with it. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.8.5 Virus Inactivation Tank (P-56/V-207)

This jacketed blending tank is used to treat the product stream with Polysorbate 80 in order to inactivate viruses in the stream. This unit is a 1,000 L blending tank made of 316L Stainless Steel with an electropolished finish. The unit is 2.2 m tall and has a diameter of 0.75 m. The working capacity of this tank is 90%. It operates at 25°C and 1.103 bar. This unit is

sterilized via CIP and SIP procedures following every batch. This surge tank is manufactured by Sharpsville Container, with a purchase cost of \$130,000.

7.8.6 Pump (P-57/PM-213)

This pump is used to transfer fluid from chemical virus inactivation tank to another sterile filtration unit. This pump, as with previous pumps, operates at 1 kW (1.34 hp). The pump is maintained at room temperature and has approximate pressure drop of 25 psi associated with it. The pump is sterilized via CIP and SIP after every batch. It can handle flow rates up to 33.3 LPM. The pump is purchased from Watson Marlow (model 825) for the cost of \$12,350.

7.8.7 Sterilizing Filter (P-58/DE-202)

This 0.2 μm filter is used to remove bacteria and other impurities from the treated product stream. It is approximately 30 inches in size with a filtration area of 1.8 m^2 . The filter operates at room temperature with a differential pressure of 0.5 bar. The filters require a type of housing for security that requires a one-time purchase from Sartorius Stedim Biotech for the cost of \$1908. The filters are disposable, and therefore need to be replaced after every batch. These filters are also purchased from Sartorius under the model name Sartopore 2 for the cost of \$608 per unit.

7.9 Cation Exchange Chromatography (BFD-09)

7.9.1 Storage Tank (P-59/V-301)

This storage tank is where Cation Buffer A is stored for use in C-301. The tank size is 4500L and made of 316L stainless steel tank with an 83% working capacity (3700L). It is 2.28 m tall and 1.52 m in diameter (1:1.5 diameter to height ratio). Operating temperature is maintained at around room temperature (25°C). The tank is sterilized using CIP and SIP techniques. The tank is manufactured by Sharpsville Container and has a purchase cost of \$117,000.

7.9.2 Storage Tank (P-60/V-302)

This storage tank is where Cation Buffer B is stored for use in C-301. The tank size is 1200L and is made of 316L stainless steel tank with an 83% working capacity (1000L). It is 1.46 m tall and 0.97 m in diameter (1:1.5 diameter to height ratio). Operating temperature is maintained at around room temperature (25°C). The tank is sterilized using CIP and SIP techniques. The tank is manufactured by Sharpsville Container and has a purchase cost of \$117,000.

7.9.3 Pump (P-61/PM-301)

This pump delivers the fluid containing the monoclonal antibody fragment from viral inactivation to MX-301 via stream S-301. It is a 316L stainless steel peristaltic pump and uses 0.01 kW of power per batch. The pump is a Watson-Marlow Bredel 825, and provides a maximum flow rate of 33.3 LPM and enough power to overcome the 45.5 ft of head required for transport. It has a purchase cost of \$12,350.

7.9.4 Pump (P-62/PM-302)

This pump delivers Cation Buffer A from V-301 to MX-301. It is a 316L stainless steel peristaltic pump and uses 0.06 kW of power per batch. The pump is a Watson-Marlow Bredel 825, and provides a maximum flow rate of 33.3 LPM and enough power to overcome the 45.5 ft of head required for transport. It has a purchase cost of \$12,350.

7.9.5 Pump (P-63/PM-303, P-64/PM-304)

This pump transports Cation Buffer B from V-302 to C-301 for elution and stripping/column regeneration. It is a 316L stainless steel peristaltic pump and uses 0.09 kW of power per batch. The pump is a Watson-Marlow Bredel 825, and provides a maximum flow rate of 33.3 LPM and enough power to overcome the 45.5 ft of head required for transport. It has a purchase cost of \$12,350.

7.9.6 Pump (P-65/PM-305, P-66/PM-306)

This pump delivers Cation Buffer A from V-301 to equilibrate and wash C-301. It is a 316L stainless steel peristaltic pump and uses 0.11 kW of power per batch (0.06 kW for equilibration, 0.05 kW for wash). The pump is a Watson-Marlow Bredel 825, and provides a maximum flow rate of 33.3 LPM and enough power to overcome the 45.5 ft of head required for transport. It has a purchase cost of \$12,350.

7.9.7 Mixer (P-67/MX-301)

This mixer forces stream S-301 and Cat-Load 2 to mix. The mixing of the antibody fragment with Cation Buffer A must be done right before entry into the column to prevent any undue denaturation or precipitation. The mixer is a joint that allows the piping of the two streams to merge. The cost is included in pricing calculations for piping.

7.9.8 Chromatography Column (P-68/C-301)

This chromatography column is operated as a cation exchange chromatography column. It is a ChromaflowTM 1000 column made by GE-Healthcare. It is made of a column tube, lid, distributor, bed support, nozzles, seals, and a stand. The distributor is made of polypropylene, the seals are made of FEP-encapsulated silicone, and the remaining parts are made of 316L stainless steel. The column has an inner diameter of 1.0m and a height of 0.5 m, giving it a column volume of 392.7 L. The cost of this chromatography column is approximately \$245,000. This cation exchange column is packed with Tosoh Toyopearl Gigacap S-650M beads, which have dynamic binding capacities of 145 mg/ml. The resin costs \$182,490 for the 110 L needed. The column and the beads can be washed using standard CIP procedures.

7.10 Anion Exchange Chromatography (BFD-10)

7.10.1 Holding Tank (P-69/V-303)

This holding tank is where the partially purified monoclonal antibody fragment (eluted product from C-301) is mixed with Anion Buffer A for use in C-302. The tank is made of 316L stainless steel and holds up to 4,200 L of fluid with an 88.8% working capacity (3730L). It is 2.3m in tall and 1.5 m in diameter. Operating temperature is maintained at around room temperature (25°C). The tank is sterilized using CIP and SIP techniques. The tank is manufactured by Sharpsville Container and has a purchase cost of \$117,000.

7.10.2 Pump (P-70/PM-307)

This pump transfers a mixed solution containing Anion Buffer A and monoclonal antibody fragments from V-303 to C-302 for further purification. It is a 316L stainless steel peristaltic pump and uses 0.11 kW of power per batch. The pump is a Watson-Marlow Bredel 840, and provides a maximum flow rate of 133.3 LPM and enough power to overcome the 45.5 ft of head required for transport. It has a purchase cost of \$18,135.

7.10.3 Chromatography Column (P-71/C-302)

This chromatography column is operated as an anion exchange chromatography column. It is a Chromaflow™ 600 column made by GE-Healthcare. It is made of a column tube, lid, distributor, bed support, nozzles, seals, and a stand. The distributor is made of polypropylene, the seals are made of FEP-encapsulated silicone, and the remaining parts are made of 316L stainless steel. The column has an inner diameter of 0.6 m and a height of 0.5 m, giving it a column volume of 141.2 L. The cost of this chromatography column is approximately \$177,000. This anion exchange column is packed with Tosoh Toyopearl SuperQ-650M beads, which have dynamic binding capacities of 140 mg/ml. The resin costs \$64,870 for the 65 L needed. Both the column and the beads can be washed using standard CIP procedures.

7.10.4 Storage Tank (P-72/V-306)

This storage tank is where the flow-through from C-302 collected. The tank is made of 316L stainless steel and holds up to 4,300 L of fluid with an 89.5% working capacity (3850L). It is 2.3 m tall and 1.5 m in diameter. Operating temperature is maintained at around room temperature (25°C). The tank is sterilized using CIP and SIP techniques. The tank is manufactured by Sharpsville Container and has a purchase cost of \$117,000.

7.10.5 Pump (P-73/PM-308)

This pump transports Anion Buffer A to V-303 from V-304 for mixing with the monoclonal antibody fragments in preparation for anion exchange chromatography. It is a 316L stainless steel peristaltic pump and uses 0.14 kW of power per batch. The pump is a Watson-Marlow Bredel 840, and provides a maximum flow rate of 133.3 LPM and enough power to overcome the 44.1 ft of head required for transport. It has a purchase cost of \$18,135.

7.10.6 Pump (P-74/PM-309, P-75/PM-310)

This pump transports Anion Buffer A to C-302 from V-304 for equilibration and washing in anion exchange chromatography. It is a 316L stainless steel peristaltic pump and uses 0.05 kW of power per batch. The pump is a Watson-Marlow Bredel 825, and provides a maximum flow rate of 33.3 LPM and enough power to overcome the 45.5 ft of head required for transport. It has a purchase cost of \$12,350.

7.10.7 Pump (P-76/PM-311)

This pump transports Anion Buffer B to C-302 from V-305 for stripping and regeneration in anion exchange chromatography. It is a 316L stainless steel peristaltic pump and uses 0.05 kW of power per batch. The pump is a Watson-Marlow Bredel 825, and provides a maximum flow rate of 33.3 LPM and enough power to overcome the 45.5 ft of head required for transport. It has a purchase cost of \$12,350.

7.10.8 Storage Tank (P-77/V-304)

This mixing tank is where Anion Buffer A is stored for use in anion exchange chromatography. The tank is made of 316L stainless steel and holds up to 4,400 L of fluid with an 88.6% working capacity (3900L). It is 2.3m tall and 1.5 m in diameter. Operating temperature is maintained at around room temperature (25°C). The tank is sterilized using CIP and SIP techniques. The tank is manufactured by Sharpsville Container and has a purchase cost of \$117,000.

7.10.9 Storage Tank (P-78/V-305)

This mixing tank is where Anion Buffer B is stored for use in anion exchange chromatography. The tank is made of 316L stainless steel and holds up to 550 L of fluid with an 86.4% working capacity (475.2L). It is 1.14m tall and 0.76 m in diameter. Operating temperature is maintained at around room temperature (25°C). The tank is sterilized using CIP and SIP techniques. The tank is manufactured by Sharpsville Container and has a purchase cost of \$117,000.

7.10.10 Pump (P-79/PM-312)

This pump transports the purified monoclonal antibody stream from V-306 to the PEGylation section (PFD -010A), where the monoclonal antibody fragments are PEGylated. It is a 316L stainless steel peristaltic pump and uses 0.04 kW of power per batch. The pump is a Watson-Marlow Bredel 825, and provides a maximum flow rate of 33.3 LPM and enough power to overcome the 50.1 ft of head required for transport. It has a purchase cost of \$12,350.

7.11 Thiol Reduction (BFD-11)

7.11.1 Diafiltration Storage Tank (P-80 / V-203)

This unit is a 4800 L jacketed storage tank with a 90% working capacity volume of 4277.24 L (height = 2.305 m, diameter = 1.537 m) to be used during the diafiltration process

between Ion Exchange Chromatography and Thiol Reduction. It is a blending tank made of electropolished 316L Stainless Steel by Sharpsville Container for a purchase cost of \$117,000. Operating conditions are 25°C and 22.038 psi. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.11.2 Diafiltration Unit (P-81 / DF-401)

This diafiltration unit will concentrate the Fab' fragments from 3.9 mg/ml in Anion Buffer 2 to 10 mg/ml in Reduction Reaction Buffer for the Thiol Reduction Reaction. This unit consists of 15 diafiltration filters, each with a membrane area of 3.0 m² to fulfill the 43.56 m² total membrane area requirement for this diafiltration process. The unit will use Sartorius Stedim Biotechnology's Sartocube® 302 144 59 30 E-BSW stabilized cellulose based filters in a Sartocon 2 Plus filter housing unit. The cutoff molecular weight for this filter is 10 kDa, and is used in order to retain the 50 kDa Fab' fragments in the retentate. The housing unit costs \$11,141 and each filter costs \$8,374, so the total cost for this unit will be \$136,751. Operating conditions are 25°C with a pressure drop of 14.5 psi. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.11.3 Pump (P-82 / PM-401)

This peristaltic pump is used to transport the Fab' fragments concentrated in the Reduction Reaction Buffer from the Diafiltration Unit to the Thiol Reduction Reactor. This pump operates at 0.12 kW (0.15 hp) and 48.36 L/min. Operating conditions are 25°C with a pressure drop of 50 psi. The pump is model 840 manufactured by Watson Marlow and costs \$18,135. This model has a maximum flow rate of 133.3 L/min and maximum power of 3.0 kW (2.2 hp). It is made of electropolished Stainless Steel 316L and will be used with Bioprene 40 mm tubing. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.11.4 Thiol Reduction Reactor (P-83 / R-401)

The reduction reaction takes place in this reactor in order to reduce any thiols that attach to the cysteine on the hinge-region end of the Fab' fragments during the purification processes. This will ensure that the thiols are available for the site-specific PEGylation reaction. This unit is a 1900 L jacketed bioreactor with a backward curved impeller for agitation and a DCS control system. It has a 90% working capacity volume of 1673.93 L (height = 2.371 m, diameter = 0.948 m). It is made of electropolished 316L Stainless Steel by ABEC for a purchase cost of \$511,000. The reaction is run at operating conditions of 37°C for 90 minutes. Validated cleaning is performed before and after every batch using CIP and SIP procedures.

7.11.5 Pump (P-84 / PM-402)

This peristaltic pump is used to transport the Fab' fragments concentrated in the Reduction Reaction Buffer from the Thiol Reduction Reactor to the next Diafiltration Unit. This pump operates at 0.12 kW (0.16 hp) and 49.11 L/min. Operating conditions are 25°C with a pressure drop of 14.5 psi. The pump is model 840 manufactured by Watson Marlow and costs \$18,135. This model has a maximum flow rate of 133.3 L/min and maximum power of 3.0 kW (2.2 hp). It is made of electropolished Stainless Steel 316L and will be used with Bioprene 40 mm tubing. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.12 PEGylation Reaction (BFD-12)

7.12.1 Diafiltration Storage Tank (P-85 / V-402)

This unit is a 1900 L jacketed storage tank with a 90% working capacity volume of 1678.37 L (height = 2.679 m, diameter = 0.893 m) to be used during the diafiltration process between Thiol Reduction and the PEGylation Reaction. It is a blending tank made of electropolished 316L Stainless Steel by Sharpsville Container for a purchase cost of \$117,000.

Operating conditions are 25°C and 22.046 psi. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.12.2 Diafiltration Unit (P-86 / DF-402)

This diafiltration unit will filter out the 2-MEA from the Reduction Reaction and keep the Fab' fragments at a concentration of 10 mg/ml in Reduction Reaction Buffer (PEGylation Reaction Buffer). This unit consists of 5 diafiltration filters, each with a membrane area of 3.0 m² to fulfill the 13.03 m² total membrane area requirement for this diafiltration process. The unit will use Sartorius Stedim Biotechnology's Sartocube® 302 144 59 30 E-BSW stabilized cellulose based filters in a Sartocon 2 Plus filter housing unit. The cutoff molecular weight for this filter is 10 kDa, and is used in order to retain the 50 kDa Fab' fragments in the retentate. The housing unit costs \$11,141 and each filter costs \$8,374, so the total cost for this unit will be \$53,011. Operating conditions are 25°C with a pressure drop of 152.68 psi. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.12.3 Pump (P-87 / PM-403)

This peristaltic pump is used to transport the Fab' fragments concentrated in the PEGylation Reaction Buffer from the Diafiltration Unit to the PEGylation Reactor. This pump operates at 0.12 kW (0.16 hp) and 49.24 L/min. Operating conditions are 25°C with a pressure drop of 14.5 psi. The pump is model 840 manufactured by Watson Marlow and costs \$18,135. This model has a maximum flow rate of 133.3 L/min and maximum power of 3.0 kW (2.2 hp). It is made of electropolished Stainless Steel 316L and will be used with Bioprene 40 mm tubing. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.12.4 PEGylation Reactor (P-88 / R-402)

In this bioreactor, the PEGylation reaction will take place to site-specifically PEGylate the Fab' fragments with a 40 kDa PEG molecule. This unit is a 2200 L jacketed bioreactor with a backward curved impeller for agitation and a DCS control system. It has a 90% working capacity

volume of 1947.83 L (height = 2.493 m, diameter = 0.997 m). It is made of electropolished 316L Stainless Steel by ABEC for a purchase cost of \$522,000. The reaction is run at operating conditions of 25°C for 2 hours. Validated cleaning is performed before and after every batch using CIP and SIP procedures. The PEG molecule that will be used is a branched maleimide polyethylene glycol molecule that will react with thiols. It is purchased from JenKem Technology USA at a bulk price of \$144/g, costing a total of \$3,285,350 per batch for the 22,814.95 g of the PEG molecular required to react with the Fab' fragments.

7.12.5 Pump (P-89 / PM-404)

This peristaltic pump is used to transport the PEGylated Fab' fragments, as well as the remaining PEG molecules and non-PEGylated Fab' fragments concentrated in the PEGylation Reaction Buffer from the PEGylation Reactor to the next Diafiltration Unit. This pump operates at 0.07 kW (0.09 hp) and 27.84 L/min. Operating conditions are 25°C with a pressure drop of 14.5 psi. The pump is model 825 manufactured by Watson Marlow and costs \$12,350. This model has a maximum flow rate of 33.3 L/min and maximum power of 1.1 kW (1.6 hp). It is made of electropolished Stainless Steel 316L and will be used with Bioprene 25 mm tubing. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.12.6 Diafiltration Storage Tank (P-90 / V-403)

This unit is an 1100 L jacketed storage tank with a 90% working capacity volume of 950.09 L (height = 2.216 m, diameter = 0.739 m) to be used during the diafiltration process between the PEGylation Reaction and Cation Exchange Chromatography. It is a blending tank made of electropolished 316L Stainless Steel by Sharpsville Container for a purchase cost of \$117,000. Operating conditions are 25°C and 26.1 psi. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.12.7 Diafiltration Unit (P-91 / DF-403)

This diafiltration unit will filter out the PEGylation Reaction Buffer and give a retentate of PEGylated Fab' fragments, excess PEG molecules, and non-PEGylated Fab' fragments in WFI to go into the Cation Exchange Chromatography. This unit consists of 3 diafiltration filters, each with a membrane area of 3.0 m^2 to fulfill the 7.39 m^2 total membrane area requirement for this diafiltration process. The unit will use Sartorius Stedim Biotechnology's Sartocube® 302 144 59 30 E-BSW stabilized cellulose based filters in a Sartocon 2 Plus filter housing unit. The cutoff molecular weight for this filter is 30 kDa, and is used in order to be sure to retain the 90 kDa PEGylated Fab' fragments in the retentate. The housing unit costs \$11,141 and each filter costs \$8,374, so the total cost for this unit will be \$36,263. Operating conditions are 25°C with a pressure drop of 26.1 psi. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.13 Cation Exchange Chromatography (BFD-13)

7.13.1 Cation Buffer 2 Storage Tank (P-92 / V-405)

This unit is a 2400 L jacketed storage tank with a 90% working capacity volume of 2113.64 L (height = 2.89 m, diameter = 0.96 m) which will be used to store prepared Cation Buffer 2 for the Elution and Stripping steps of the Cation Ion Exchange Chromatography. It is a blending tank made of electropolished 316L Stainless Steel by Sharpville Container for a purchase cost of \$117,000. Operating conditions are 25°C and 132.2 psi. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.13.2 Cation Buffer 1 Storage Tank (P-93 / V-404)

This unit is a 2400 L jacketed storage tank with a 90% working capacity volume of 2113.64 L (height = 2.89 m, diameter = 0.96 m) which will be used to store prepared Cation Buffer 2 for the Elution and Stripping steps of the Cation Ion Exchange Chromatography. It is a

blending tank made of electropolished 316L Stainless Steel by Sharpsville Container for a purchase cost of \$117,000. Operating conditions are 25°C and 132.226 psi. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.13.3 Pump (P-94 / PM-405)

This peristaltic pump is used to transport the mixture of PEGylated Fab' fragments, excess PEG molecules, and non-PEGylated Fab' fragments in WFI during the Load step of the Cation Exchange Chromatography. This pump operates at 0.12 kW (0.16 hp) and 48.79 L/min. Operating conditions are 25°C with a pressure drop of 14.5 psi. The pump is model 840 manufactured by Watson Marlow and costs \$18,135. This model has a maximum flow rate of 133.3 L/min and maximum power of 3.0 kW (2.2 hp). It is made of electropolished Stainless Steel 316L and will be used with Bioprene 40 mm tubing. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.13.4 Pump (P-95 / PM-406)

This peristaltic pump is used to transport Cation Buffer 1 from the storage tank in order to be mixed with the incoming PEGylated Fab' stream before the Load step of the Cation Exchange Chromatography. This pump operates at 0.29 kW (0.38 hp) and 119.83 L/min. Operating conditions are 25°C with a pressure drop of 14.5 psi. The pump is model 840 manufactured by Watson Marlow and costs \$18,135. This model has a maximum flow rate of 133.3 L/min and maximum power of 3.0 kW (2.2 hp). It is made of electropolished Stainless Steel 316L and will be used with Bioprene 40 mm tubing. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.13.5 Pump (P-96 / PM-410)

This peristaltic pump is used to transport Cation Buffer 2 from the storage tank to the Cation Exchange Chromatography Column during the Stripping step. This pump operates at 0.06 kW (0.08 hp) and 25.18 L/min. Operating conditions are 25°C with a pressure drop of 14.5 psi.

The pump is model 825 manufactured by Watson Marlow and costs \$12,350. This model has a maximum flow rate of 33.3 L/min and maximum power of 1.6 kW (1.1 hp). It is made of electropolished Stainless Steel 316L and will be used with Bioprene 25 mm tubing. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.13.6 Pump (P-97 / PM-411)

This peristaltic pump is used to transport Cation Buffer 2 from the storage tank to the Chromatography Column during the Elution step. This pump operates at 0.02 kW (0.03 hp) and 9.21 L/min. Operating conditions are 25°C with a pressure drop of 14.5 psi. The pump is model 825 manufactured by Watson Marlow and costs \$12,350. This model has a maximum flow rate of 33.3 L/min and maximum power of 1.6 kW (1.1 hp). It is made of electropolished Stainless Steel 316L and will be used with Bioprene 25 mm tubing. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.13.7 Pump (P-98 / PM-409)

This peristaltic pump is used to transport Cation Buffer 1 from the storage tank to the Cation Exchange Chromatography Column during the Washing step. This pump operates at 0.04 kW (0.06 hp) and 18.88 L/min. Operating conditions are 25°C with a pressure drop of 14.5 psi. The pump is model 825 manufactured by Watson Marlow and costs \$12,350. This model has a maximum flow rate of 33.3 L/min and maximum power of 1.6 kW (1.1 hp). It is made of electropolished Stainless Steel 316L and will be used with Bioprene 25 mm tubing. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.13.8 Pump (P-99 / PM-407)

This peristaltic pump is used to transport Cation Buffer 1 from the storage tank to the Cation Exchange Chromatography Column during the Equilibration step. This pump operates at 0.06 kW (0.08 hp) and 25.18 L/min. Operating conditions are 25°C with a pressure drop of 14.5 psi. The pump is model 825 manufactured by Watson Marlow and costs \$12,350. This model has

a maximum flow rate of 33.3 L/min and maximum power of 1.6 kW (1.1 hp). It is made of electropolished Stainless Steel 316L and will be used with Bioprene 25 mm tubing. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.13.9 Mixer (P-100 / MX-102)

This mixing step will be a joint in the piping of the system which will mix the incoming Fab' stream with Cation Buffer 1 from the storage tank immediately before the Loading step of the Cation Exchange Chromatograph. This must be done to ensure that the PEGylated Fab' fragments do not denature. Price will be incorporated into the cost of piping.

7.13.10 Chromatography Column (P-101 / C-401)

This unit is a Cation Exchange Chromatography Column which goes through a process of Equilibration, Washing, Loading, Elution and Stripping. It is a 154.46 L (height = 0.787 m, diameter = 1.0 m) Chromaflow™ 1000 column made by GE Healthcare which will be purchased for \$249,000. The distributor is made of polypropylene, the seals are made of FEP-encapsulated silicone, and the column, lid, bed support, nozzles, and stand are made of 316L stainless steel. The 154.46 L bed will be packed with GE Healthcare MacroCap SP Resin with a dynamic binding capacity of 150 mg/ml and a linear velocity of 120 cm/h, which will cost \$290,230 at a price of \$1,879 per liter. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.14 Final Filtration (BFD-14)

7.14.1 Pump (P-102/PM-501)

This pump transports the purified monoclonal antibody stream from the PEGylation section (PFD -010A) to the diafiltration holding tank V-501. It is a 316L stainless steel peristaltic pump and uses 0.02 kW of power per batch. The pump is a Watson-Marlow Bredel 825, and

provides a maximum flow rate of 33.3 LPM and enough power to overcome the 45.5 ft of head required for transport. It has a purchase cost of \$12,350.

7.14.2 Holding Tank (P-103/V-501)

This holding tank is used to store fluid for diafiltration. The tank is made of 316L stainless steel and holds up to 370 L of fluid with a 90% working capacity (333L). It is 1.0m tall and 0.68m in diameter. Operating temperature is maintained at around room temperature (25°C). The tank is sterilized using CIP and SIP techniques. The tank is manufactured by Sharpville Container and has a purchase cost of \$117,000.

7.14.3 Diafiltration (P-104/DF-501)

Diafiltration cassettes will be provided by Sartorius Stedim Biotechnology. The membrane is composed of the cellulose-based Hydrosart, is about 3.0 m² in area. The cutoff molecular weight for this filter is 30 kDa, and is used in order to retain the 90 kDa PEGylated Fab' fragments in the retentate. The housing unit costs \$11,141 and each filter costs \$8,374, so the total cost for this unit will be \$36,263. Operating conditions are 25°C with a pressure drop of 26.1 psi. Cleaning is performed before and after every batch using CIP and SIP procedures.

7.14.4 Peristaltic Pump (P-105/PM-502)

This pump transports the purified monoclonal antibody stream diafiltration to viral filtration. It is a 316L stainless steel peristaltic pump and uses 0.036 kW of power per batch. The pump is a Watson-Marlow Bredel 825, and provides a maximum flow rate of 33.3 LPM. It has a purchase cost of \$12,350.

7.14.5 Retrovirus Filtration (P-106/DE-501)

This 50 nm normal flow filter is used to remove larger viral particles, such as retroviruses and certain bacteriophages, while allowing the PEGylated monoclonal antibody fragment (10nm) to pass through. The Viresolve NFR Cartridge filter is manufactured by Millipore and is made of polyethersulfone with a filtration area of 0.43m². The filter costs \$1,459 and the housing for it

costs \$1,340. A new filter will be used for each batch to ensure sterility and to maximize filtration of the virus.

7.14.6 Parvovirus Filtration (P-107/DE-502)

This 20 nm normal flow filter is used to remove parvoviruses from the product stream, while allowing the PEGylated monoclonal antibody fragment (10nm) to pass through. The Viresolve NFP Cartridge filter is manufactured by Millipore and is made of modified polyvinylidene fluoride (PVDF) with a filtration area of 0.42m². The filter costs \$3,963 and the housing for it costs \$1,340. A new filter will be used for each batch to ensure sterility and to maximize filtration of the virus.

7.14.7 Disposable Container Storage (P-108/DCS-101)

Dispensing the final product into 50 L bags is done by the SciLog Fillmaster system. It contains a peristaltic pump, whose maximum flow rate is 14.6 LPM, and distributes liquid accurately into sterile 50 L HyClone Labtainer Bags made of a special HyQ CX5-14 film. The SciLog Fillmaster system costs \$10,000 and the sterile bags cost \$49.05 each.

7.14.8 Refrigeration (P-109/EC-501)

Freezing down of the PEGylated monoclonal antibody is necessary to keep the product stable for as long as possible. Effective temperatures for long term storage range from -20°C to -80°C. The freezing is done using an ultra cold freezer, which can reach temperatures up to -85°C. The freezer can hold up to 1050 L (or 21 bags) and requires 10.85 kW per batch. Manufactured by Cincinnati Sub-Zero, the freezer is made of 304 grade stainless steel and costs \$45,000.

8.0 Additional Equipment and Pricing

There are several pieces of equipment that are integral to the operation of the monoclonal antibody production plant, but are not found on the process flow diagrams. These pieces of equipment are described in this section, along with a description of the spare equipment that will be purchased.

8.1 Incubators for T-flasks and Roller Bottles

Mammalian cells need to live at a very specific temperature to survive and proliferate. The incubators are used to control the temperature of the t-flasks and roller bottles. The total cost of the incubators, which are manufactured by Thermo Scientific, is \$15,000. Electricity consumption per batch for the incubators is 49.9 kWh.

8.2 Roller Bottle Apparatus

The roller bottle apparatus is a system that is used to rotate the roller bottles to ensure the cultures receive enough oxygen to grow. The apparatus is used inside the roller bottle incubator. Manufactured by Cole-Parmer, the total cost of the apparatus costs \$6500.

8.3 Biosafety Cabinet

A biosafety cabinet is needed to provide a sterile environment for aseptic handling and transfer of mammalian cells into T-flasks and roller bottles. Manufactured by Thermo Scientific, the biosafety cabinet costs \$10,000.

8.4 Air Generator (HVAC Equipment)

Purified air will be provided by an HVAC system, supplying pure air to bioreactors, clean rooms, and other process equipment. This cost of the system is \$1.2 million and requires 100 kW of power per hour.

8.5 Clean Steam Generator

The clean steam generator is used to produce steam from WFI and clean process equipment with steam-in-place procedures. It has a power requirement of 4.1 kW and costs \$200,000.

8.6 CIP Skids

CIP, or Clean-In-Place, is a technique used to clean process equipment. A CIP skid contains the cleaning solutions and equipment and is portable, as it can be wheeled around to different pieces of process equipment. Three CIP skids, manufactured by Sani-matic, will be needed for this process and each one will cost \$80,000. Power consumption totals to about 7.5 kW per batch.

8.7 Buffer Transfer Bags

Buffer transfer bags are used to transfer media or buffer to certain processing steps. These disposable bags are manufactured by HyClone and will cost approximately \$70,000 a year.

8.8 Filter Integrity Tester

The filter integrity tester is used to test sterile and viral filters before use to ensure that they are not clogged, torn, or unusable. Even though the filters used are single-use, filter testing is performed to prevent loss of product and time. The filter integrity tester from Millipore, or the Integritest Exacta Automatic Filter Integrity Test Instrument, has a purchase cost of \$16,500.

8.9 Tube Fuser

In using sterile, single-use, equipment, it is necessary to connect tubing of process equipment, sterile containers, and bags to transfer liquid. Sartorius Stedim Biotech's Sterile Tube Fuser is a fully automatic device that cuts and fuses tube ends together to ensure sterility. It costs \$15,300.

8.10 Tube Sealer

The tube sealer is used to seal plastic tubing to prevent leaks from the bags that are used throughout the process. It is a fully automated unit and can be used on many types of plastic tubing. It is produced by Sartorius Stedim Biotech and the cost of the tube sealer is \$10,200.

8.11 Water Treatment Package

The water treatment package is used to generate USP grade water from tap water. The package costs \$100,000 and uses 7.5 kW per batch.

8.12 WFI Still

The WFI still further purifies the water from the water treatment package to produce WFI. WFI is used throughout the process to ensure sterility of the product and process equipment. The still costs \$350,000 and is manufactured by the Paul Mueller Co. It requires 37.3 kW per batch.

8.13 Biowaste and Neutralization Waste Tanks

Two separate tanks are necessary to collect the wastes generated by the process. All wastes potentially carrying living cells are sent to the biowaste tank, while the rest are sent to the neutralization tank. The biowaste tank is 5,000 L, while the neutralization tank is 35,000 L. These tanks will be made of 316L stainless steel and manufactured by Sharpsville Container for \$125,000 each.

8.14 Biowaste Inactivation System

This system kills any remaining biomass in the biowaste tank. This includes all CIP and SIP washes, from the main bioreactors and primary recovery. The system costs \$270,000 and uses 12 kW per batch.

8.15 Waste Neutralization System

The waste neutralization system operates by adjusting the pH of process waste in the neutralization tank to 7.0. This allows the wastes to be sent to the sewer. The cost of the system is \$100,000 and requires 12kW for operation.

8.16 Blood Gas Analyzer

A blood gas analyzer is needed to analyze the contents of the media. This includes nutrients, metabolites, gases, cell density, cell viability, osmolality, and even IgG concentration. With the BioProfile Flex, manufactured by Nova Biomedical, up to 16 assays can be performed within minutes. The total cost of the system is \$45,000

8.17 Laboratory Information Management System (LIMS)

The Laboratory Information Management system, or LIMS, is software that is used to manage a laboratory. It manages samples, users, instruments, and many laboratory functions. The cost of a LIMS is \$450,000 and is provided by STARLIMS.

8.19 Portable Pump on Cart

A portable pump on cart is used in case a connected pump breaks down or malfunctions. This pump will easily replace the broken pump until it can be fixed. An extra Watson-Marlow Bredel 840 pump and a cart will cost \$12,500.

8.20 Final Packaging

The monoclonal antibody produced by plant will not be ready for dosing of patients, as the product requires further packaging. The product will be shipped out to a facility that will lyophilize the frozen antibodies in septum bottles, allowing the longer shelf-life at room temperature. Final packaging, including both shipping and lyophilization, will be performed by Quality BioResources, Inc., and costs \$270,000 per batch.

9.0 Unit Specification Sheets

The following pages contain the unit specification sheets for the equipment used in our manufacturing facility. Equipment models and prices have been obtained through direct contact with vendors.

T-Flask (P-1 / TFR-101)

Function: Non-treated, sterile flasks for the suspension and growth of cell cultures.

Vendor: Nunc International

PFD Reference: PFD-01

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Amino Acids	0.00267
	Glucose	0.01132
	Glutamine	0.00131
	Inorganic Salts	0.02742
	Other Media	0.00024
	Vitamins	0.00011
	WFI	2.11021
	Total	2.15309

<u>Characteristics:</u>	Model:	Nunc EasyFlask 159933
	Material of Construction:	Polystyrene
	Cap:	Filter
	Flask Type:	Non-treated, Sterile
	Total Volume:	225 ml
	Suggested Working Volume:	70 ml
	Additional Features:	Disposable
<u>Operating Conditions:</u>	Temp:	37 °C
	Pressure:	1 bar
	Duration:	4 days
	Number of Containers:	20

Purchase Cost: \$205.01/(30 flasks)

Reference Page: 466

Roller Bottle (P-2 / RBR-101)

Function: Non-treated, sterile bottles for the suspension and growth of cell cultures.

Vendor: Nunc International

PFD Reference: PFD-01

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	0.01363
Biomass	0.00030
Dead Biomass	0.00003
Glucose	0.05770
Glutamine	0.00667
<u>Materials Handled:</u> Inorganic Salts	0.13976
Lactate	0.00021
MAB	0.00006
Other Media	0.00121
Vitamins	0.00057
Water	0.00053
WFI	10.80021
Total	11.02088

<u>Characteristics:</u> Model:	Nunc Standard Roller Bottle 186022
Material of Construction:	PETG
Flask Type:	Non-treated, Sterile
Culture Area:	1800 cm ²
Suggested Working Volume:	200-1000
Additional Features:	Disposable

<u>Operating Conditions:</u> Temp:	37 °C
Pressure:	1 bar
Duration:	4 days
Number of Containers:	11

Purchase Cost: \$426.75/(22 bottles)

Reference Page: 468

Bag Bioreactor (P-3 / BBS-101)

Function:	A pre-sterilized disposable bioreactor chamber equipped with ports for sterile aeration, seeding, harvesting, sampling and analysis. The rocker unit is used to control and monitor temperature, pH, aeration rate, and rocking speed to obtain proper cell growth.
Vendor:	Sartorius Stedim Biotech
PFD Reference:	PFD-01

<u>Operation:</u>	Batch	
<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Amino Acids	0.08843
	Biomass	0.00189
	Dead Biomass	0.00019
	Glucose	0.37423
	Glutamine	0.04329
	Inorganic Salts	0.90654
	Lactate	0.00134
	MAB	0.00039
	Other Media	0.00783
	Vitamins	0.00370
	Water	0.00339
	WFI	70.04777
	Total	71.47899
<u>Characteristics:</u>	Model:	BIOSTAT® CultiBag RM
	Type:	Rocker 20/50 (Optical Package)
	Bag Size:	20 L
	Max Working Volume:	10 L
	Min Working Volume:	2 L
	Sterilization:	Disposable Bags
<u>Operating Conditions:</u>	Temp:	37 °C
	Pressure:	1 bar
	pH:	7.0
	DO:	50%
	Duration:	4 Days
	Number In Use Per Batch:	8
<u>Purchase Cost:</u>	Rocker and Control Unit: \$33,000 (Quote from Applikon) Disposable Bag: \$447/bag (Quote from Applikon)	
<u>Reference Page:</u>	483	

Bag Bioreactor (P-4 / BBS-102)

Function:	A pre-sterilized disposable bioreactor chamber equipped with ports for sterile aeration, seeding, harvesting, sampling and analysis. The rocker unit is used to control and monitor temperature, pH, aeration rate, and rocking speed to obtain proper cell growth.
Vendor:	Sartorius Stedim Biotech
PFD Reference:	PFD-01

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	0.39911
Biomass	0.01393
Dead Biomass	0.00143
Glucose	1.68901
Glutamine	0.19538
Inorganic Salts	4.09140
Lactate	0.00988
MAB	0.00286
Other Media	0.03535
Vitamins	0.01671
Water	0.02501
WFI	316.91374
Total	323.39381

Materials Handled:

<u>Characteristics:</u>	Model:	BIOSTAT® CultiBag RM
	Type:	Rocker 200 (Optical Package)
	Bag Size:	100 L
	Max Working Volume:	50 L
	Min Working Volume:	10 L
	Sterilization:	Disposable Bags
	Temp:	37 °C
	Pressure:	1 bar
<u>Operating Conditions:</u>	pH:	7.0
	DO:	50%
	Duration:	4 Days
	Number In Use Per Batch:	7

Purchase Cost: Rocker and Control Unit: \$39,000 (Quote from Applikon)
Disposable Bag: \$447/bag (Quote from Applikon)

Reference Page: 483

Storage/Mixing Tank (P-5 / MP-101)

Function: Tank used to store and mix powdered serum free media with water for injection prior to being pumped through a sterile filter.

Vendor: Sharpsville Container

PFD Reference: PFD-02

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	1.36298
Glucose	5.76797
Glutamine	0.66722
<u>Materials Handled:</u> Inorganic Salts	13.97219
Other Media	0.12071
Vitamins	0.05707
WFI	648.69449
Total	670.64263

<u>Characteristics:</u>	Material of Construction:	Stainless Steel 316
	Volume:	1000 L
	Height:	2.2 m
	Diameter:	0.8 m
	Working Capacity:	70%
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Pressure:	1 bar

Purchase Cost: \$117,000

Reference Page: 508

Pump (P-6 / PM-101)

Function: Pump to transfer fluid from first media prep storage tank to first sterile filter.

Vendor: Watson Marlow

PFD Reference: PFD-02

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Amino Acids	1.36298
	Glucose	5.76797
	Glutamine	0.66722
	Inorganic Salts	13.97219
	Other Media	0.12071
	Vitamins	0.05707
	WFI	648.69449
	Total	670.64263

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	1.34 hp/ 1 kW
	Pressure Change	25 psi

Purchase Cost: \$12,350

Reference Pages: 493, 505

Sterilization Filter (P-7 / DE-101)

Function: 0.2 µm filter to remove bacteria and other impurities from the serum free media prior to feeding the first seed bioreactor.

Vendor: Sartorius Stedim Biotech

PFD Reference: PFD-02

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Amino Acids	1.36298
	Glucose	5.76797
	Glutamine	0.66722
	Inorganic Salts	13.97219
	Other Media	0.12071
	Vitamins	0.05707
	WFI	648.69449
	Total	670.64263

<u>Characteristics:</u>	Model:	Sartopore 2 0.2 µm
	Size:	30''
	Filtration Area:	1.8 m ² (18 ft ²)
	Max. Differential Pressure:	5 bar (75 psi) at 20°C

<u>Operating Conditions:</u>	Temp:	25 °C
	Differential Pressure:	0.5 bar (7.5 psi)

<u>Purchase Cost:</u>	Filter Housing:	\$1,908
	Filter Membrane:	\$608/unit

Reference Page: 491

Pump (P-8 / PM-102)

Function: Pump to transfer fluid from first sterile filter to first seed bioreactor.

Vendor: Watson Marlow

PFD Reference: PFD-02

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Amino Acids	1.36298
	Glucose	5.76797
	Glutamine	0.66722
	Inorganic Salts	13.97219
	Other Media	0.12071
	Vitamins	0.05707
	WFI	648.69449
	Total	670.64263

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	1.34 hp/ 1 kW
	Pressure Change	25 psi

Purchase Cost: \$12,350

Reference Pages: 493, 505

Seed Bioreactor (P-9 / SBR-101)

Function: Bioreactor used for continued cell growth and production of monoclonal antibodies.

Vendor: ABEC

PFD Reference: PFD-02

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	1.75135
Biomass	0.07321
Dead Biomass	0.0075
Glucose	7.41151
Glutamine	0.85734
<u>Materials Handled:</u> Inorganic Salts	17.95346
Lactate	0.0519
MAB	0.01502
Other Media	0.15511
Vitamins	0.07333
Water	0.13141
WFI	965.60863
Total	994.08977

<u>Characteristics:</u>	Material of Construction:	Stainless Steel 316
	Volume:	1500 L
	Height:	2.3 m
	Diameter:	0.9 m
	Working Capacity:	70%
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	37°C
	Pressure:	1 bar
	pH:	7.0
	DO:	50%
	Duration:	4 days

Purchase Cost: \$495,000

Reference Page: 507

Pump (P-10 / PM-103)

Function: Pump to transfer fluid from first seed bioreactor to second seed bioreactor.

Vendor: Watson Marlow

PFD Reference: PFD-03

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Amino Acids	0.18
	Biomass	8.77
	Dead Biomass	0.90
	Glucose	0.74
	Glutamine	0.09
	Inorganic Salts	1.80
	Lactate	6.22
	MAB	1.80
	Other Media	0.00
	Oxygen	0.02
	Vitamins	0.01
	Water	15.74
	WFI	969.06
	Total	1005.31

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C (Room Temperature)
	Power:	1.34 hp/ 1 kW
	Pressure Change	25 psi

Purchase Cost: \$12,350

Reference Pages: 493, 505

Storage/Mixing Tank (P-11 / MP-102)

Function: Tank used to store and mix powdered serum free media with water for injection prior to being pumped to a sterile filter.

Vendor: Sharpsville Container

PFD Reference: PFD-03

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	4.17654
Glucose	17.67465
Glutamine	2.04456
<u>Materials Handled:</u> Inorganic Salts	42.81462
Other Media	0.3699
Vitamins	0.17486
WFI	2011.29215
Total	2078.54728

<u>Characteristics:</u>	Material of Construction:	Stainless Steel 316
	Volume:	3000 L
	Height:	3.3 m
	Diameter:	1.1 m
	Working Capacity:	70%
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Pressure:	1 bar

Purchase Cost: \$120,000

Reference Page: 508

Pump (P-12 / PM-104)

Function: Pump to transfer fluid from second media prep storage tank to second sterile filter.

Vendor: Watson Marlow

PFD Reference: PFD-03

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Amino Acids	4.17654
	Glucose	17.67465
	Glutamine	2.04456
	Inorganic Salts	42.81462
	Other Media	0.3699
	Vitamins	0.17486
	WFI	2011.29215
	Total (kg/batch)	2078.54728

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	1.34 hp/ 1 kW
	Pressure Change	25 psi

Purchase Cost: \$12,350

Reference Pages: 493, 505

Sterilization Filter (P-13 / DE-102)

Function: 0.2 µm filter to remove bacteria and other impurities from the serum free media prior to feeding the second seed bioreactor.

Vendor: Sartorius Stedim Biotech

PFD Reference: PFD-03

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	4.17654
Glucose	17.67465
Glutamine	2.04456
Inorganic Salts	42.81462
Other Media	0.3699
Vitamins	0.17486
WFI	2011.29215
Total	2078.54728

Materials Handled:

<u>Characteristics:</u>	Model:	Sartopore 2 0.2 µm
	Size:	30''
	Filtration Area:	1.8 m ² (18 ft ²)
	Max. Differential Pressure:	5 bar (75 psi) at 20°C

<u>Operating Conditions:</u>	Temp:	25 °C
	Differential Pressure:	0.5 bar (7.5 psi)

Purchase Cost: Filter Housing: \$1,908
Filter Membrane: \$608/unit

Reference Page: 491

Pump (P-14 / PM-105)

Function: Pump to transfer fluid from second sterile filter to second seed bioreactor.

Vendor: Watson Marlow

PFD Reference: PFD-03

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	4.17654
Glucose	17.67465
Glutamine	2.04456
<u>Materials Handled:</u> Inorganic Salts	42.81462
Other Media	0.3699
Vitamins	0.17486
WFI	2011.29215
Total	2078.54728

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	1.34 hp/ 1 kW
	Pressure Change	25 psi

Purchase Cost: \$12,350

Reference Pages: 493, 505

Seed Bioreactor (P-15 / SBR-102)

Function: Bioreactor used for continued cell growth and production of monoclonal antibodies.

Vendor: ABEC

PFD Reference: PFD-03

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	4.52681
Biomass	7.80284
Dead Biomass	0.79941
Glucose	19.15695
Glutamine	2.21603
<u>Materials Handled:</u> Inorganic Salts	46.40531
Lactate	5.53213
MAB	1.60111
Other Media	0.40092
Vitamins	0.18953
Water	14.00684
WFI	2976.90078
Total	3079.53866

<u>Characteristics:</u>	Material of Construction:	Stainless Steel 316
	Volume:	4500 L
	Height:	3.3 m
	Diameter:	1.3 m
	Working Capacity:	70%
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	37°C
	Pressure:	1 bar
	pH:	7.0
	DO:	50%
	Duration:	4 days

Purchase Cost: \$585,000

Reference Page: 507

Pump (P-16 / PM-106)

Function: Pump to transfer fluid from second seed bioreactor to production bioreactor.

Vendor: Watson Marlow

PFD Reference: PFD-04

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Amino Acids	0.90536
	Biomass	27.78205
	Dead Biomass	2.84632
	Glucose	3.83139
	Glutamine	0.4432
	Inorganic Salts	9.28106
	Lactate	19.6972
	MAB	5.70075
	Other Media	0.08019
	Vitamins	0.03791
	Water	49.87146
	WFI	2976.90077
	Total	3097.37766

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C (Room Temperature)
	Power:	1.34 hp/ 1 kW
	Pressure Change	25 psi

Purchase Cost: \$12,350

Reference Pages: 493, 505

Storage/Mixing Tank (P-17 / MP-103)

Function: Tank used to store and mix powdered serum free media with water for injection prior to being pumped to a sterile filter (P-19).

Vendor: Sharpsville Container

PFD Reference: PFD-04

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	10.74057
Glucose	45.45284
Glutamine	5.25786
<u>Materials Handled:</u> Inorganic Salts	110.10379
Other Media	0.95126
Vitamins	0.44969
WFI	5222.19771
Total	5395.15372

<u>Characteristics:</u>	Material of Construction:	Stainless Steel 316
	Volume:	7700 L
	Height:	4.5 m
	Diameter:	1.5 m
	Working Capacity:	70%
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Pressure:	1 bar

Purchase Cost: \$130,000

Reference Page: 508

Pump (P-18 / PM-107)

Function: Pump to transfer fluid from storage tank (P-17) to sterile filter (P-19).

Vendor: Watson Marlow

PFD Reference: PFD-04

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	10.74057
Glucose	45.45284
Glutamine	5.25786
Inorganic Salts	110.10379
Other Media	0.95126
Vitamins	0.44969
WFI	5222.19771
Total	5395.15372

Materials Handled:

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	1.34 hp/ 1 kW
	Pressure Change	25 psi

Purchase Cost: \$12,350

Reference Pages: 493, 505

Sterilization Filter (P-19 / DE-103)

Function: 0.2 µm filter to remove bacteria and other impurities from the serum free media prior to feeding the production bioreactor.

Vendor: Sartorius Stedim Biotech

PFD Reference: PFD-04

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	10.74057
Glucose	45.45284
Glutamine	5.25786
Inorganic Salts	110.10379
Other Media	0.95126
Vitamins	0.44969
WFI	5222.19771
Total	5395.15372

Materials Handled:

<u>Characteristics:</u>	Model:	Sartopore 2 0.2 µm
	Size:	30''
	Filtration Area:	1.8 m ² (18 ft ²)
	Max. Differential Pressure:	5 bar (75 psi) at 20°C

<u>Operating Conditions:</u>	Temp:	25 °C
	Differential Pressure:	0.5 bar (7.5 psi)

Purchase Cost: Filter Housing: \$1,908
Filter Membrane: \$608/unit

Reference Page: 491

Pump (P-20 / PM-108)

Function: Pump to transfer fluid from sterile filter (P-19) to the production bioreactor.

Vendor: Watson Marlow

PFD Reference: PFD-04

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	10.74057
Glucose	45.45284
Glutamine	5.25786
Inorganic Salts	110.10379
Other Media	0.95126
Vitamins	0.44969
WFI	5222.19771
Total	5395.15372

Materials Handled:

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	1.34 hp/ 1 kW
	Pressure Change	25 psi

Purchase Cost: \$12,350

Reference Pages: 493, 505

Storage/Mixing Tank (P-21 / MP-104)

Function: Tank used to store and mix powdered serum free media with water for injection for fed batch considerations prior to being pumped to a sterile filter (P-23).

Vendor: Sharpsville Container

PFD Reference: PFD-04

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	1.36
Glucose	5.77
Glutamine	0.67
Inorganic Salts	13.97
Other Media Components	0.12
Vitamins	0.06
WFI	908.165
Total	674.10

Materials Handled:

<u>Characteristics:</u>	Material of Construction:	Stainless Steel 316
	Volume:	1600 L
	Height:	2.6 m
	Diameter:	0.9 m
	Working Capacity:	70%
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Pressure:	1 bar

Purchase Cost: \$117,000

Reference Page: 508

Pump (P-22 / PM-109)

Function: Pump to transfer fluid from media prep storage tank (P-21) to sterile filter (P-23).

Vendor: Watson Marlow

PFD Reference: PFD-04

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	17.12144
Glucose	72.45596
Glutamine	8.38151
<u>Materials Handled:</u> Inorganic Salts	175.5155
Other Media	1.51639
Vitamins	0.71684
WFI	897.8898
Total	1173.597

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	1.34 hp/ 1 kW
	Pressure Change	25 psi

Purchase Cost: \$12,350

Reference Pages: 493, 505

Sterilization Filter (P-23 / DE-104)

Function: 0.2 µm filter to remove bacteria and other impurities from the serum free media prior to feeding the production bioreactor (fed batch).

Vendor: Sartorius Stedim Biotech

PFD Reference: PFD-04

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	17.12144
Glucose	72.45596
Glutamine	8.38151
<u>Materials Handled:</u> Inorganic Salts	175.5155
Other Media	1.51639
Vitamins	0.71684
WFI	897.8898
Total	1173.597

<u>Characteristics:</u>	Model:	Sartopore 2 0.2 µm
	Size:	30''
	Filtration Area:	1.8 m ² (18 ft ²)
	Max. Differential Pressure:	5 bar (75 psi) at 20°C

<u>Operating Conditions:</u>	Temp:	25 °C
	Differential Pressure:	0.5 bar (7.5 psi)

<u>Purchase Cost:</u>	Filter Housing: \$1,908
	Filter Membrane: \$608/unit

Reference Page: 491

Pump (P-24 / PM-110)

Function: Pump to transfer fluid from the sterile filter (P-23) tank to production bioreactor.

Vendor: Watson Marlow

PFD Reference: PFD-04

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Amino Acids	17.12144
	Glucose	72.45596
	Glutamine	8.38151
	Inorganic Salts	175.5155
	Other Media	1.51639
	Vitamins	0.71684
	WFI	897.8898
	Total	1173.597

<u>Characteristics:</u>	Model:	Watson-Marlow Breidel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	1.34 hp/ 1 kW
	Pressure Change	25 psi

Purchase Cost: \$12,350

Reference Pages: 493, 505

Production Bioreactor (P-25 / PBR-101)

Function: Fed batch bioreactor used for continued cell growth and production of monoclonal antibodies at a 3.5 g/l titer.

Vendor: ABEC

PFD Reference: PFD-04

Operation: Fed Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	28.76737
Biomass	27.78205
Dead Biomass	2.84632
Glucose	121.74019
Glutamine	14.08257
Inorganic Salts	294.90032
Lactate	19.6972
MAB	5.70075
Other Media	2.54784
Vitamins	1.20444
Water	49.87146
WFI	9096.9883
Total	9666.12881

Materials Handled:

Material of Construction:	Stainless Steel 316
Volume:	14000 L
Height:	4.8 m
Diameter:	2.0 m
Working Capacity:	70%
Sterilization:	SIP/CIP
Number of Staggered Vessels:	2
Temp:	37 °C
Pressure:	1 bar
pH:	7.0
DO:	50%
Duration:	9 days

Characteristics:

Operating Conditions:

Purchase Cost: \$661,000 (x2)

Reference Page: 507

Surge Tank (P-26 / V-201)

Function: To store output of production bioreactor (P-25 / PBR-101)

Vendor: Sharpsville Container

PFD Reference: PFD-05

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	3.48470
Biomass	167.26423
Dead Biomass	17.13653
Glucose	14.74685
Glutamine	1.70588
Inorganic Salts	35.72240
Lactate	118.58868
Monoclonal Antibodies	34.32188
Other Media Components	0.30863
Vitamins	0.14590
Water	300.25541
WFI	9096.98830
Total	9790.669

Materials Handled:

<u>Characteristics:</u>	Capacity:	11,000 L
	Inside Diameter:	1.67 m
	Height:	5.00 m
	Interior Construction:	316L Electropolished Stainless Steel
	Sterilization:	SIP / CIP

<u>Operating Conditions:</u>	Temperature:	25°C
	Pressure:	1.103 bar

Purchase Cost: \$ 129,000

Reference Page: 508

Pump (P-27 / PM-201)

Function: To transfer fluid from bioreaction surge tank (P-26 / V-201) to centrifugation unit (P-28 / DS-201)

Vendor: Watson Marlow

PFD Reference: PFD-05

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	3.49
Biomass	167.26
Dead Biomass	17.14
Glucose	14.75
Glutamine	1.71
Inorganic Salts	35.72
Lactate	118.59
Monoclonal Antibodies	34.32
Other Media Components	0.31
Vitamins	0.15
Water	300.26
WFI	9096.99
Total	9790.67

Materials Handled:

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	1.34 hp/ 1 kW
	Pressure Change	25 psi

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Centrifuge (P-28 / DS-201)

Function: To remove cells from the stream containing the monoclonal antibody product

Vendor: Alfa-Laval

PFD Reference: PFD-05

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Amino Acids	3.49
	Biomass	167.26
	Dead Biomass	17.14
	Glucose	14.75
	Glutamine	1.71
	Inorganic Salts	35.72
	Lactate	118.59
	Monoclonal Antibodies	34.32
	Other Media Components	0.31
	Vitamins	0.15
	Water	300.26
	WFI	9096.99
	Total	9790.67

<u>Characteristics:</u>	Model:	BTAX 215H-31 CEP
	Centrifuge Type:	Hermetic
	Material of Construction:	Stainless Steel 316
	Max bowl speed:	6,065 rpm
	Power:	13-28 kW
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Throughput:	2,000 L/h

Purchase Cost: \$ 421,000

Reference Page: 510

Pump (P-29 / PM-202)

Function: To transfer fluid from centrifugation unit (P-28 / DS-201) to sterile filter (P-30 / DE – 201)

Vendor: Watson Marlow

PFD Reference: PFD-05

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Amino Acids	3.15
	Biomass	3.35
	Dead Biomass	15.49
	Glucose	13.33
	Glutamine	1.54
	Inorganic Salts	32.28
	Lactate	107.16
	Monoclonal Antibodies	31.02
	Other Media Components	0.28
	Vitamins	0.13
	Water	271.33
	WFI	8220.53
	Total	8699.58

<u>Characteristics:</u>	Model: Pump Type: Material of Construction: Flow Rate: Power: Sterilization:	Watson-Marlow Bredel 825 Peristaltic Stainless Steel 316 33.3 LPM 1.5 – 5.0 hp SIP/CIP
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<u>Operating Conditions:</u>	Temp: Power: Pressure Change	25 °C 1.34 hp/ 1 kW 25 psi
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Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Sterilizing Filter (P-30 / DE-201)

Function: To sterilize supernatant of centrifugation process and remove bacteria from stream

Vendor: Sartorius Stedim Biotech

PFD Reference: PFD-05

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	3.15
Biomass	3.35
Dead Biomass	15.49
Glucose	13.33
Glutamine	1.54
Inorganic Salts	32.28
Lactate	107.16
Monoclonal Antibodies	31.02
Other Media Components	0.28
Vitamins	0.13
Water	271.33
WFI	8220.53
Total	8699.58

Materials Handled:

Characteristics:

Model:	Sartopore 2 0.2 µm
Size:	30''
Filtration Area:	1.8 m ² (18 ft ²)
Max. Differential Pressure:	5 bar (75 psi) at 20°C

Operating Conditions:

Temp:	25 °C
Differential Pressure:	0.5 bar (7.5 psi)

Purchase Cost:

Filter Housing:	\$1908
Filter Membrane:	\$ 608/ unit

Reference Page: 491

Pump (P-31 / PM-203)

Function: To transfer fluid from sterile filter (P-30 / DE-201) to centrifugation pool tank (P-32 / V-202)

Vendor: Watson Marlow

PFD Reference: PFD-05

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Amino Acids	3.15
	Biomass	0.00
	Dead Biomass	15.48
	Glucose	13.32
	Glutamine	1.54
	Inorganic Salts	32.27
	Lactate	107.12
	Monoclonal Antibodies	31.00
	Other Media Components	0.28
	Vitamins	0.13
	Water	271.22
	WFI	8217.36
	Total	8692.87

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	1.34 hp/ 1 kW
	Pressure Change	25 psi

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Centrifugation Pool Tank (P-32 / V-202)

Function: To store sterilized supernatant from centrifugation process

Vendor: Sharpsville Container

PFD Reference: PFD-05

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	3.15
Dead Biomass	15.48
Glucose	13.32
Glutamine	1.54
Inorganic Salts	32.27
<u>Materials Handled:</u> Lactate	107.12
Monoclonal Antibodies	31.00
Other Media Components	0.28
Vitamins	0.13
Water	271.22
WFI	8217.36
Total	8692.87

<u>Characteristics:</u>	Capacity:	10,000 L
	Inside Diameter:	1.6 m
	Height:	4.8 m
	Interior Construction:	316L Electropolished Stainless Steel
	Sterilization:	SIP / CIP

<u>Operating Conditions:</u>	Temperature:	25°C
	Pressure:	1.103 bar

Purchase Cost: \$ 17,000

Reference Page: 508

Pump (P-33 / PM-204)

Function: To transfer fluid from centrifugation pool tank (P-32 / V-202) to the diafiltration storage tank (P-35 / DF-201)

Vendor: Watson Marlow

PFD Reference: PFD-06

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	3.15
Dead Biomass	15.48
Glucose	13.32
Glutamine	1.54
Inorganic Salts	32.27
<u>Materials Handled:</u> Lactate	107.12
Monoclonal Antibodies	31.00
Other Media Components	0.28
Vitamins	0.13
Water	271.22
WFI	8217.36
Total	8692.87

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	1.34 hp/ 1 kW
	Pressure Change	25 psi

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Diafiltration Storage Tank (P-34 / V-203)

Function: To store sterilized supernatant from centrifugation process prior to diafiltration.

Vendor: Sharpsville Container

PFD Reference: PFD-06A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	3.15
Dead Biomass	15.48
Glucose	13.32
Glutamine	1.54
Inorganic Salts	32.27
<u>Materials Handled:</u> Lactate	107.12
Monoclonal Antibodies	31.00
Other Media Components	0.28
Vitamins	0.13
Water	271.22
WFI	8217.36
Total	8692.87

<u>Characteristics:</u>	Capacity:	10,000 L
	Inside Diameter:	1.6 m
	Height:	4.8 m
	Interior Construction:	316L Electropolished Stainless Steel
	Sterilization:	SIP / CIP

<u>Operating Conditions:</u>	Temperature:	25°C
	Pressure:	1.103 bar

Purchase Cost: \$ 117,000

Reference Page: 508

Diafiltration Unit (P-35 / DF-201)

Function: To concentrate the monoclonal antibody-containing stream to prepare it for the cleavage reaction

Vendor: Sartorius Stedim Biotechnology

PFD Reference: PFD-06

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	3.15
Dead Biomass	15.48
Glucose	13.32
Glutamine	1.54
HCl	0.00
Impurities	0.00
Inorganic Salts	32.31
<u>Materials Handled:</u> Lactate	107.12
MAB	31.00
Other Media Components	0.28
Sodium Acetate	0.00
Vitamins	0.13
Water	271.22
WFI	8217.36
TOTAL (kg/batch)	8692.92

<u>Characteristics:</u> Cassette Model:	Sartocube® 302 144 59 30 E-BSW
Membrane:	Hydrosart (stabilized cellulose based)
Filter Area per Cassette:	3.0 m ²
Filter holder:	Sartocon 2 Plus
Maximum feed pressure:	58 psi (4 bar)
Sterilization:	SIP/CIP

<u>Operating Conditions:</u> Number of units:	2
Total Filter area:	14.901 m ²
Filter MWCO:	30 kDa
Temp:	25 °C
Pressure Change:	43.5 psi

Purchase Cost: Diafiltration Housing: \$ 11,141
Diafiltration Cartridges: \$ 8374 / 3m²

Reference Pages: 514, 516, 518, 520

Pump (P-36 / PM-205)

Function: To transport the concentrated monoclonal-antibody containing-stream from the diafiltration unit (P-35 / DF-201) to the Pepsin Cleavage Reactor (P-37 / R-201)

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-06

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	0.14
Dead Biomass	0.69
Glucose	0.60
Glutamine	0.07
Impurities	0.50
Inorganic Salts	1.45
<u>Materials Handled:</u> Lactate	4.80
MAB	30.07
Other Media Components	0.01
Sodium Acetate	6.70
Vitamins	0.01
Water	12.14
WFI	2833.00
TOTAL (kg/batch)	2890.17

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	1.34 hp/ 1 kW
	Pressure Change	50 psi

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Pepsin Cleavage Bioreactor (P-37 / R-201)

Function:	To cleave the monoclonal antibody into F(ab) ₂ and Fc fragments using immobilized pepsin
Vendor:	Abec
PFD Reference:	PFD-06

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
<u>Materials Handled:</u>	Amino Acids	0.14
	Dead Biomass	0.69
	Glucose	0.60
	Glutamine	0.07
	Impurities	0.50
	Inorganic Salts	1.45
	Lactate	4.80
	MAB	30.07
	Other Media Components	0.01
	Sodium Acetate	6.70
	Vitamins	0.01
	Water	12.14
	WFI	2833.00
	TOTAL (kg/batch)	2890.17

<u>Characteristics:</u>	Material of Construction:	316L Stainless Steel, Electropolished
	Mode of agitation	Backward curved impeller
	Mode of Drive:	Top mechanical agitation
	Mode of Control:	DCS control sistem
	Volume:	9,000 L
	Height:	4.06 m
	Diameter	1.62 m
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	37°C
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<u>Purchase Cost:</u>	\$ 622,000
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<u>Reference Page:</u>	507
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Pump (P-38 / PM-206)

Function: Transport product-containing stream from the cleavage bioreactor (P-37 / R-201) to the plate and frame filtration unit (P-39/ PFF-201)

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-06

Operation: Batch

Input: Quantity (kg/batch):

Amino Acids	0.14
Dead Biomass	0.69
F(ab') ₂	15.24
Glucose	0.60
Glutamine	0.07
Impurities	0.50
Inorganic Salts	1.45
Lactate	4.80

Materials Handled:

MAB	1.50
MAb Fc Fragments	13.33
Other Media Components	0.01
Pepsin	1540.43
Sodium Acetate	10.88
TRIS HCl	0.00
Vitamins	0.01
Water	12.14
WFI	2364.28
TOTAL (kg/batch)	3966.06

Characteristics:

Model:	Watson-Marlow Bredel 825
Pump Type:	Peristaltic
Material of Construction:	Stainless Steel 316
Flow Rate:	33.3 LPM
Power:	1.5 – 5.0 hp
Sterilization:	SIP/CIP

Operating Conditions:

Temperature:	25 °C
Power:	12.07 hp/ 9 kW
Pressure Change:	25 psi

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Plate and Frame Filtration Unit (P-39 / PFF-201)

Function: To remove the immobilized pepsin from the product stream

Vendor: Pall Corporation

PFD Reference: PFD-06

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	0.14
Dead Biomass	0.69
F(ab') ₂	15.24
Glucose	0.60
Glutamine	0.07
Impurities	0.50
Inorganic Salts	1.45
Lactate	4.80
MAB	1.50
MAB Fc Fragments	13.33
Other Media Components	0.01
Pepsin	1540.43
Sodium Acetate	10.88
TRIS HCl	0.00
Vitamins	0.01
Water	12.14
WFI	2364.28
TOTAL (kg/batch)	3966.06

Materials Handled:

Characteristics:

Model:	MEMBRAp [®] lan [®] DGM
Plate size:	1000 mm x 1000 mm
Material of Construction:	Stainless Steel 316L
Chassis Size:	800 K 100
No. Filter Plates	29
Sterilization:	SIP/CIP

Operating Conditions:

Temperature:	25 °C
Filter Area:	24.4 m ²

Purchase Cost: \$ 74,000

Reference Page: 522

Pump (P-40 / PM-207)

Function: To transport the concentrated monoclonal-antibody containing-stream from the P&F filter (P-39 / UF-201) to the protein A chromatography column (P-40 / C-201)

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-07

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	0.13
Dead Biomass	0.65
F(ab') ₂	14.31
Glucose	0.56
Glutamine	0.07
Impurities	0.47
Inorganic Salts	1.36
Lactate	4.51
<u>Materials Handled:</u> MAB	1.41
MAB Fc Fragments	12.53
Other Media Components	0.01
Sodium Acetate	10.22
TRIS HCl	160.75
Vitamins	0.01
Water	11.41
WFI	4040.65
TOTAL (kg/batch)	4259.03

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25 °C
	Power:	9 kW/ 12.07 hp
	Pressure Change	25 psi

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Diafiltration Storage Tank (P-41 / V-204)

Function: To store F(ab')₂ fragments from P&F Filtration prior to Diafiltration process.

Vendor: Sharpsville Container

PFD Reference: PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	0.13
Dead Biomass	0.65
F(ab') ₂	16.67
Glucose	0.56
Glutamine	0.07
Impurities	0.44
Inorganic Salts	1.35
Lactate	4.48
<u>Materials Handled:</u> MAB	1.32
MAB Fc Fragments	8.34
Other Media Components	0.01
Oxygen	0.00
Sodium Acetate	6.27
TRIS HCl	147.46
Vitamins	0.01
Water	11.35
WFI	3486.58
TOTAL (kg/batch)	3685.68

<u>Characteristics:</u>	Capacity:	4027.01 L
	Inside Diameter:	1.196 m
	Height:	3.587 m
	Interior Construction:	316L Electropolished Stainless Steel
	Sterilization:	SIP / CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Pressure:	22.04 psi

Purchase Cost: \$1 17,000

Reference Page: 508

Diafiltration Unit (P-42 / DF-202)

Function: To concentrate the F(ab')₂ fragments from 3.56 mg/ml to 10 mg/ml in Reduction Reaction Buffer to prepare for the Thiol Reduction Reaction.

Vendor: Sartorius Stedim Biotechnology

PFD Reference: PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	3.15
Dead Biomass	15.48
Glucose	13.32
Glutamine	1.54
Phosphate	14477.03
Impurities	0.00
Inorganic Salts	32.31
<u>Materials Handled:</u> Lactate	107.12
MAB	31.00
Other Media Components	0.28
EDTA, Sodium	1134.87
Vitamins	0.13
Water	271.22
WFI	10242.90
TOTAL (kg/batch)	26330.40

Characteristics:

Cassette Model:	Sartocube® 302 144 59 30 E-BSW
Membrane:	Hydrosart (stabilized cellulose based)
Filter Area per Cassette:	3.0 m ²
Filter holder:	Sartocon 3
Maximum feed pressure:	58 psi (4 bar)
Sterilization:	SIP/CIP

Operating Conditions:

Number of units:	15
Total Filter area:	43.185 m ²
Filter MWCO:	30 kDa
Temp:	25 °C
Pressure Change:	14.5 psi

Purchase Cost:

Ultrafiltration Housing:	\$ 11,141
Ultrafiltration Cartridges:	\$ 125,610

Reference Pages: 514, 516, 518, 520

Pump (P-43 / PM-208)

Function: To transport F(ab')₂ fragments from the Diafiltration System (P-41 / V-402, P-42 / DF-202) to the Thiol Reduction Reactor (P-44 / R-202).

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Amino Acids	0.01
Dead Biomass	0.03
EDTA, Sodium	178.18
F(ab') ₂	16.67
Glucose	0.03
Impurities	0.27
Inorganic Salts	0.07
<u>Materials Handled:</u> Lactate	0.22
MAB	0.06
MAB Fc Fragments	0.41
Sodium Acetate	0.31
Sodium Phosphate	2272.91
TRIS HCl	7.28
Water	0.56
WFI	411.49
TOTAL (kg/batch)	2888.50

<u>Characteristics:</u> Model:	Watson-Marlow Bredel 840
Pump Type:	Peristaltic
Material of Construction:	Stainless Steel 316L
Flow Rate:	133.3 L/min
Power:	2.2 hp / 3.0 kW
Tubing:	Bioprene 40 mm
Sterilization:	SIP/CIP

<u>Operating Conditions:</u> Temp:	25 °C
Power:	4.11 hp/3.07 kW
Volumetric Throughput:	186.80 L/min
Pressure Change	14.5 psi

Purchase Cost: \$18,135

Reference Pages: 493, 505

Disulfide Reduction Reactor (P-44 / R-202)

Function: To reduce the hinge region disulfide bonds in the F(ab')₂ molecules to produce Fab' molecules, which retain a hinge region cysteine that facilitates site-specific PEGylation.

Vendor: Abec

PFD Reference: PFD-10A

Operation:

Batch

Input:**Quantity (kg/batch):**

2-MEA	8.00
Amino Acids	0.01
Dead Biomass	0.03
EDTA, Sodium	178.18
F(ab') ₂	16.67
Glucose	0.03
Glutamine	0.00
Impurities	0.27
Inorganic Salts	0.07
Lactate	0.22
MAB	0.06
MAb Fab Fragments	0.00
Other Media Components	0.41
Sodium Acetate	0.31
Sodium Phosphate	2272.91
TRIS HCl	7.28
Water	0.56
WFI	411.49
TOTAL (kg/batch)	2896.50

Materials Handled:

Material of Construction:	316L Stainless Steel, Electropolished
Mode of agitation	Backward curved impeller
Mode of Drive:	Top mechanical agitation
Mode of Control:	DCS control system
Volume:	1589.93 L
Height:	2.330 m
Diameter	0.932 m
Sterilization:	SIP/CIP

Characteristics:**Operating Conditions:**

Temperature:	37°C
Incubation Time:	90 minutes

Purchase Cost: \$ 508,000

Reference Page: 507

Pump (P-45 / PM-209)

Function: To transport Fab' molecules in Reduction Reactor Buffer from the Thiol Reduction Reactor (P-44 / R-202) to the Diafiltration System (P-46 / V-205).

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	8.00
Amino Acids	0.01
Dead Biomass	0.03
EDTA, Sodium	178.18
F(ab') ₂	16.67
Glucose	0.03
Impurities	0.27
Inorganic Salts	0.07
<u>Materials Handled:</u> Lactate	0.22
MAB	0.06
Other Media Components	0.41
Sodium Acetate	0.31
Sodium Phosphate	2272.91
TRIS HCl	7.28
Water	0.56
WFI	411.49
TOTAL (kg/batch)	2896.50

<u>Characteristics:</u> Model:	Watson-Marlow Bredel 840
Pump Type:	Peristaltic
Material of Construction:	Stainless Steel 316L
Flow Rate:	133.3 L/min
Power:	2.2 hp / 3.0 kW
Tubing:	Bioprene 40 mm
Sterilization:	SIP/CIP
Temp:	25 °C
<u>Operating Conditions:</u> Power:	0.15 hp/ 0.11 kW
Volumetric Throughput:	46.65 L/min
Pressure Change	14.5 psi

Purchase Cost: \$18,135

Reference Pages: 493, 505

Diafiltration Storage Tank (P-46 / V-205)

Function: To store Fab' fragments from the Thiol Reduction Reaction prior to Protein-A Chromatography.

Vendor: Sharpsville Container

PFD Reference: PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	8.00
Amino Acids	0.01
Dead Biomass	0.03
EDTA, Sodium	178.18
Glucose	0.03
Glutamine	0.00
Impurities	0.27
Inorganic Salts	0.07
Lactate	0.22
MAB	0.06
MAb Fab Fragments	16.67
MAb Fc Fragments	0.41
Sodium Acetate	0.31
Sodium Phosphate	2272.91
TRIS HCl	7.28
Water	0.56
WFI	411.49
TOTAL (kg/batch)	2896.50

Materials Handled:

Characteristics: Capacity: 1597.82 L
Inside Diameter: 0.879 m
Height: 2.636 m
Interior Construction: 316L Electropolished Stainless Steel
Sterilization: SIP / CIP

Operating Conditions: Temp: 25 °C
Pressure: 22.04 psi

Purchase Cost: \$117,000

Reference Page: 508

Diafiltration Unit (P-47 / DF-203)

Function: To filter out 2-MEA and small Fc fragments and to switch the Fab' fragments from Reduction Reaction Buffer to WFI while maintaining a concentration of 10 mg/ml.

Vendor: Sartorius Stedim Biotechnology

PFD Reference: PFD-10A

Operation:

Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	8.00
Dead Biomass	0.03
EDTA, Sodium	178.18
Glucose	0.03
Glutamine	0.00
Impurities	0.27
Inorganic Salts	0.07
Lactate	0.22
MAB	0.06
MAB Fab Fragments	16.67
MAB Fc Fragments	0.41
Sodium Acetate	0.31
Sodium Phosphate	2272.91
TRIS HCl	7.28
Water	0.56
WFI	3781.30
TOTAL (kg/batch)	6266.31

Materials Handled:**Characteristics:**

Cassette Model: Sartocube® 302 144 59 30 E-BSW
 Membrane: Hydrosart (stabilized cellulose based)
 Filter Area per Cassette: 3.0 m²
 Filter holder: Sartocon 3
 Maximum feed pressure: 58 psi (4 bar)
 Sterilization: SIP/CIP

Operating Conditions:

Number of units: 5
 Total Filter area: 12.415 m²
 Filter MWCO: 10 kDa
 Temp: 25 °C
 Pressure Change: 14.5 psi

Purchase Cost:

Diafiltration Housing: \$ 11,141
 Diafiltration Cartridges: \$ 41,870

Reference Pages:

514, 516, 518, 520

Pump (P-48 / PM-210)

Function: To transport the Fab' fragments from the Diafiltration System (P-46 / V-205, P-47 / DF-203) to the Protein-A Chromatography (P-49 / C-201).

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	1.08
Amino Acids	0.00
Dead Biomass	0.00
EDTA, Sodium	24.11
Glucose	0.00
Glutamine	0.00
Impurities	0.18
Inorganic Salts	0.01
Lactate	0.03
MAB	0.01
MAB Fab Fragments	16.67
MAB Fc Fragments	0.06
Sodium Phosphate	307.61
TRIS HCl	0.99
Vitamins	0.00
Water	0.08
WFI	1281.16
TOTAL (kg/batch)	1632.02

Materials Handled:

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Max Flow Rate:	33.3 L/min
	Max Power:	1.6 hp / 1.1 kW
<u>Operating Conditions:</u>	Tubing:	Bioprene 25 mm
	Sterilization:	SIP/CIP
	Temp:	25 °C
	Power:	0.28 hp/ 0.21 kW
	Volumetric Throughput:	25.09 L/min
	Pressure Change	14.5 psi

Purchase Cost: \$12,350

Reference Pages: 493, 505

Protein A Chromatography Column (P-49 / C-201)

Function: To purify the antibody Fab fragments from the mainstream fluid

Vendor: Amersham biosciences (GE corporation)

PFD Reference: PFD-07

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
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2-MEA	0.01
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Dead Biomass	0.01
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EDTA, Sodium	25.57
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Glucose	0.01
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Impurities	0.23
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Inorganic Salts	0.03
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Lactate	0.08
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MAB	0.02
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<u>Materials Handled:</u> MAb Fab Fragments	14.31
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MAb Fc Fragments	0.23
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Sodium Acetate	0.19
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Sodium Chloride	756.15
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Sodium Phosphate	238.00
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TRIS Base	0.19
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TRIS HCl	3.50
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Water	0.21
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WFI	3942.67
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TOTAL (kg/batch)	4981.43
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<u>Characteristics:</u> Column Model:	BPG 450
Inner Diameter:	450 mm
Tube Height:	1000 mm
Material of Construction:	Stainless Steel 316
Max. Bed Volume:	90.6 L
Max Pressure:	2.5 bar
Column Media:	nProtein A Sepharose Fast Flow
Binding Capacity:	50 mg antibody / ml media
Working Flow Velocity:	30–300 cm/h
Temperature stability:	4-40°C

<u>Operating Conditions:</u> Temperature:	4 °C
Pressure:	1.01 bar

Purchase Cost: \$ 190,000 for BPG column, \$7,000 / L Protein A Media

Reference Pages: 529, 537

Pump (P-50 / PM-211)

Function: To transport the concentrated antibody solution from the protein A chromatography column (P-49/ C-201) to the sterile filtration unit (P-51 / DE-202)

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-07

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	0.01
Acetic-Acid	0.20
Dead Biomass	0.01
EDTA, Sodium	25.20
Glucose	0.01
Impurities	0.18
Inorganic Salts	0.03
<u>Materials Handled:</u> Lactate	0.08
MAb Fab Fragments	14.31
Sodium Acetate	0.19
Sodium Chloride	755.97
Sodium Phosphate	238.00
TRIS HCl	2.94
Water	0.21
WFI	3791.15
TOTAL (kg/batch)	4828.50

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25 °C
	Power:	1.34 hp/ 1kW
	Pressure Change	25 psi

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Sterilizing Filter (P-51 / DE-202)

Function: To sterilize supernatant of Protein A chromatography and remove bacteria from stream

Vendor: Sartorius Stedim Biotech

PFD Reference: PFD-05

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	0.01
Acetic-Acid	0.20
Dead Biomass	0.01
EDTA, Sodium	25.20
Glucose	0.01
Impurities	0.18
Inorganic Salts	0.03
<u>Materials Handled:</u> Lactate	0.08
MAB Fab Fragments	14.31
Sodium Acetate	0.19
Sodium Chloride	755.97
Sodium Phosphate	238.00
TRIS HCl	2.94
Water	0.21
WFI	3791.15
TOTAL (kg/batch)	4828.50

<u>Characteristics:</u>	Model:	Sartopore 2 0.2 μ m
	Size:	30''
	Filtration Area:	1.8 m ² (18 ft ²)
	Max. Differential Pressure:	5 bar (75 psi) at 20°C

<u>Operating Conditions:</u>	Temp:	25 °C
	Differential Pressure:	0.5 bar (7.5 psi)

Purchase Cost: Filter Housing: \$1908
Filter Membrane: \$ 608/ unit

Reference Page: 491

Pump (P-52/ PM-209)

Function: To transport the product containing-stream from the sterile filtration unit (P-51 / DE-202) to the diafiltration system

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-07

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	0.01
Acetic-Acid	0.20
EDTA, Sodium	25.20
Glucose	0.01
Impurities	0.18
Inorganic Salts	0.03
Lactate	0.08
<u>Materials Handled:</u> MAb Fab Fragments	14.31
Sodium Acetate	0.19
Sodium Chloride	755.97
Sodium Phosphate	238.00
TRIS HCl	2.94
Water	0.21
WFI	3791.14
TOTAL (kg/batch)	4828.48

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25 °C
	Power:	1.34 hp/ 1kW
	Pressure Change	25 psi

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Diafiltration Storage Tank (P-53 / V-206)

Function: To store product containing stream prior to diafiltration

Vendor: Sharpsville Container

PFD Reference: PFD-06A

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	2-MEA	0.01
	Acetic-Acid	0.20
	EDTA, Sodium	25.20
	Glucose	0.01
	Impurities	0.18
	Inorganic Salts	0.03
	Lactate	0.08
	MAb Fab Fragments	14.31
	Sodium Acetate	0.19
	Sodium Chloride	755.97
	Sodium Phosphate	238.00
	TRIS HCl	2.94
	Water	0.21
	WFI	3791.14
	TOTAL (kg/batch)	4828.48

Characteristics:

Capacity:	10,000 L
Inside Diameter:	1.6 m
Height:	4.8 m
Interior Construction:	316L Electropolished Stainless Steel
Sterilization:	SIP / CIP

Operating Conditions:

Temperature:	25°C
Pressure:	1.103 bar

Purchase Cost: \$ 117,000

Reference Page: 508

Diafiltration Unit (P-54 / DF-204)

Function:	To concentrate the monoclonal antibody-containing stream to prepare it for the cleavage reaction
Vendor:	Sartorius Stedim Biotechnology
PFD Reference:	PFD-06

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	0.01
Acetic-Acid	0.20
EDTA, Sodium	25.20
Glucose	0.01
Impurities	0.18
Inorganic Salts	0.03
Lactate	0.08
<u>Materials Handled:</u> MAb Fab Fragments	14.31
Sodium Acetate	0.19
Sodium Chloride	755.97
Sodium Phosphate	238.00
TRIS HCl	2.94
Water	0.21
WFI	3791.14
TOTAL (kg/batch)	4828.48

<u>Characteristics:</u>	Cassette Model:	Sartocube® 302 144 59 30 E-BSW
	Membrane:	Hydrosart (stabilized cellulose based)
	Filter Area per Cassette:	3.0 m ²
	Filter holder:	Sartocon 3
	Maximum feed pressure:	58 psi (4 bar)
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Number of units:	6
	Total Filter area:	14.901 m ²
	Filter MWCO:	10 kDa
	Temp:	25 °C
	Pressure Change:	43.5 psi

<u>Purchase Cost:</u>	Ultrafiltration Housing: \$ 11,141
	Ultrafiltration Cartridges: \$ 8374 / 3m ²

Reference Page: 514, 516, 518, 520

Pump (P-55/ PM-213)

Function: To transport the product containing-stream from diafiltration system to the chemical inactivation tank (P-56 / V-207)

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-07

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Acetic-Acid	0.01
Dead Biomass	0.00
EDTA, Sodium	0.67
Impurities	0.09
MAB Fab Fragments	14.31
<u>Materials Handled:</u> Sodium Acetate	0.01
Sodium Chloride	20.19
Sodium Phosphate	6.36
TRIS HCl	0.08
Water	0.01
WFI	837.19
TOTAL (kg/batch)	878.90

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25 °C
	Power:	1.34 hp/ 1kW
	Pressure Change	25 psi

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Virus Inactivation Tank (P-56/ V-207)

Function: To treat the product stream with Polysorbate 80 to inactivate viruses

Vendor: Sharpsville Container

PFD Reference: PFD-06A

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Acetic-Acid	0.01
	Dead Biomass	0.00
	EDTA, Sodium	0.67
	Impurities	0.09
	MAB Fab Fragments	14.31
	Sodium Acetate	0.01
	Sodium Chloride	20.19
	Sodium Phosphate	6.36
	TRIS HCl	0.08
	Water	0.01
	WFI	837.19
	TOTAL (kg/batch)	878.90

<u>Characteristics:</u>	Capacity:	1,000 L
	Inside Diameter:	0.75 m
	Height:	2.2 m
	Interior Construction:	316L Electropolished Stainless Steel
	Sterilization:	SIP / CIP

<u>Operating Conditions:</u>	Temperature:	25°C
	Pressure:	1.103 bar

Purchase Cost: \$ 117,000

Reference Page: 508

Pump (P-57/ PM-214)

Function: To transport the product containing-stream virus inactivation tank to the sterile filtration unit (P-58/DE-203)

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-07

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Acetic-Acid	0.01
	EDTA, Sodium	0.67
	Impurities	0.09
	MAB Fab Fragments	14.31
	Polysorbate 80	0.09
<u>Materials Handled:</u>	Sodium Acetate	0.01
	Sodium Chloride	20.19
	Sodium Phosphate	6.36
	TRIS HCl	0.08
	Water	0.01
	WFI	837.28
	TOTAL (kg/batch)	879.08

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316
	Flow Rate:	33.3 LPM
	Power:	1.5 – 5.0 hp
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25 °C
	Power:	1.34 hp/ 1kW
	Pressure Change	25 psi

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Sterilizing Filter (P-58 / DE-203)

Function: To sterilize supernatant of centrifugation process and remove bacteria from stream

Vendor: Sartorius Stedim Biotech

PFD Reference: PFD-05

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
Acetic-Acid	0.01
EDTA, Sodium	0.67
Impurities	0.09
MAb Fab Fragments	14.31
Polysorbate 80	0.09
<u>Materials Handled:</u> Sodium Acetate	0.01
Sodium Chloride	20.19
Sodium Phosphate	6.36
TRIS HCl	0.08
Water	0.01
WFI	837.28
TOTAL (kg/batch)	879.08

Characteristics:

Model:	Sartopore 2 0.2 µm
Size:	30''
Filtration Area:	1.8 m ² (18 ft ²)
Max. Differential Pressure:	5 bar (75 psi) at 20°C

Operating Conditions:

Temp:	25 °C
Differential Pressure:	0.5 bar (7.5 psi)

Purchase Cost:

Filter Housing:	\$1908
Filter Membrane:	\$ 608/ unit

Reference Page: 491

Storage Tank (P-59 / V-301)

Function: To hold buffer solution for cation exchange chromatography

Vendor: Sharpsville Container

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	MES Buffer	36.0861
	WFI	3660.4993
	Total	3716.2655

<u>Characteristics:</u>	Material of Construction:	Stainless Steel 316L
	Total Volume:	4129.18 L
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25 °C
	Pressure:	1 bar

Purchase Cost: \$ 110,000

Reference Page: 508

Storage Tank (P-60 / V-302)

Function: To hold buffer solution for cation exchange chromatography

Vendor: Sharpsville Container

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	MES Buffer	9.0985
	Sodium Chloride	54.4783
	WFI	932.2062
	Total	974.4692

<u>Characteristics:</u>	Material of Construction:	Stainless Steel 316L
	Total Volume:	1082.75 L
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25 °C
	Operating Pressure:	1 bar

Purchase Cost: \$ 114,000

Reference Page: 508

Pump (P-61 / PM-301)

Function: To transfer fluid from chemical virus inactivation to cation chromatography column

Vendor: Watson –Marlow Bredel

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	2-MEA	0.028
	Amino Acids	0.00002
	Acetic Acid	0.00132
	EDTA, Sodium	0.62195
	Glucose	0.0001
	Glutamine	0.00001
	Impurities	0.06612
	Inorganic Salts	0.00023
	Lactate	0.00077
	MAb Fab Fragments	16.67308
	Polysorbate 80	0.02949
	Sodium Acetate	0.00108
	Sodium Phosphate	7.93396
	Tris HCl	0.02542
	Water	0.00196
	WFI	269.4751
	Total	294.859

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	Up to 33.33 LPM
	Tubing:	Bioprene, 25 mm
	Sterilization:	SIP
	Pressure Change:	1 bar
<u>Operating Conditions:</u>	Pump Head:	45.5 ft
	Max. Flow Rate:	2.61 LPM
	Power Consumption:	0.0134 hp

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Pump (P-62 / PM-302)

Function: To transfer buffer solution from storage tank to cation exchange chromatography column

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-09

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
<u>Materials Handled:</u>	MES Buffer	25.47882
	WFI	2584.52118
	Total	2610.0

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	Up to 33.33 LPM
	Tubing:	Bioprene, 25 mm
	Sterilization:	SIP

<u>Operating Conditions:</u>	Pressure Change:	1 bar
	Pump Head:	45.5 ft
	Max. Flow Rate:	23.57 LPM
	Power Consumption:	0.056 kW

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Pump (P-63 / PM-303, P-64 / PM-304)

Function: To transfer buffer solution from storage tank to cation exchange chromatography column

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-09

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
<u>Materials Handled:</u>	MES Buffer	9.10
	Sodium Chloride	54.48
	WFI	932.21
	Total	995.78

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	Up to 33.33 LPM
	Tubing:	Bioprene, 25 mm
	Sterilization:	SIP

<u>Operating Conditions:</u>	Pressure Change:	1 bar
	Pump Head:	45.5 ft
	Max. Flow Rate:	26.18 LPM
	Power Consumption:	0.09 kW

Purchase Cost: \$12,350

Reference Pages: 493, 505

Pump (P-65 / PM-305, P-66 / PM-306)

Function: To transfer buffer solution from storage tank to cation exchange chromatography column

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	MES Buffer	10.61
	WFI	1075.98
	Total	1086.59

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	Up to 33.33 LPM
	Tubing:	Bioprene, 25 mm
	Sterilization:	SIP

<u>Operating Conditions:</u>	Pressure Change:	1 bar
	Pump Head:	45.5 ft
	Max. Flow Rate:	26.18 LPM
	Power Consumption:	0.11 kW

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Cation Chromatography Column (P-68 /C-301)

Function: To purify and isolate antigen binding fragments from impurities

Vendor: GE-Amersham

PFD Reference: PFD-09

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	0.0279
Amino Acids	0.0000
Acetic-Acid	0.0013
EDTA, Sodium	0.6220
Glucose	0.0001
Glutamine	0.0000
Impurities	0.0661
Inorganic Salts	0.0002
Lactate	0.0008
<u>Materials Handled:</u> MAb Fab Fragments	16.6731
MES	25.4788
Other Media Components	0.0000
Polysorbate 80	0.0295
Sodium Acetate	0.0011
Sodium Phosphate	7.9340
TRIS HCl	0.0254
Vitamins	0.0000
Water	0.0020
WFI	2853.9963
Total	2904.8586

<u>Characteristics:</u>	Model:	Chromaflo 1000
	Material of Construction:	Stainless Steel 316, PE
	Column Volume:	436.95 L
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Bed Volume:	109.24L
	Resin:	Toyopearl Gigacap S-650M

Purchase Cost: \$ 245,000

Reference Page: 529

Holding Tank (P-69 / V-303)

Function: To hold and mix product from cation exchange chromatography with buffer solutions in preparation for anion exchange chromatography

Vendor: Sharpsville Container

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Impurities	0.0079
	MAb Fab Fragments	15.0475
	MES	0.5332
	Sodium Chloride	11.9266
	WFI	3685.3208
	TRIS Base	14.7608
	Total	3728.0859

<u>Characteristics:</u>	Material of Construction:	Stainless Steel 316L
	Total Volume:	4148.45 L
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25 °C
	Operating Pressure:	1 bar

Purchase Cost: \$ 117,000

Reference Page: 508

Pump (P-70 / PM-307)

Function: To transfer mixed solution from storage tank to anion exchange chromatography column

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Impurities	0.0079
	MAB Fab Fragments	15.0475
	MES Buffer	0.5332
	Sodium Chloride	11.9266
	WFI	3685.3208
	TRIS Base	14.7608
	Total	3728.0859

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 840
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	Up to 133.33 LPM
	Tubing:	Bioprene, 40mm
	Sterilization:	SIP

<u>Operating Conditions:</u>	Pressure Change:	1 bar
	Pump Head:	44.1 ft
	Max. Flow Rate:	44.74 LPM
	Power Consumption:	0.143 hp

Purchase Cost: \$ 18,135

Reference Pages: 493, 505

Anion Exchange Chromatography Column (P-71 / C-302)

Function: To remove impurities and purify antigen binding fragments

Vendor: GE-Amersham

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Impurities	0.0079
	MAb Fab Fragments	15.0475
	MES Buffer	0.5332
	Sodium Chloride	11.9266
	TRIS Base	14.7608
	WFI	3685.3208
	Total	3727.5968

<u>Characteristics:</u>	Model:	Chromaflo 600
	Material of Construction:	Stainless Steel 316L, PE
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25 °C
	Resin:	Toyopearl SuperQ-650M

Purchase Cost: \$ 177,000

Reference Page: 529

Anion Exchange Pool Tank (P-72 / V-306)

Function: To collect product from anion exchange chromatography

Vendor: Sharpsville Container

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Impurities	0.0004
	MAb Fab Fragments	15.0098
	MES	0.5332
	Sodium Chloride	12.2159
	TRIS Base	15.2497
	WFI	3800.2578
	Total	3843.7711

<u>Characteristics:</u>	Material of Construction:	Stainless Steel 316L
	Total Volume:	4277.22 L
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25 °C
	Operating Pressure:	1 bar

Purchase Cost: \$ 121,000

Reference Page: 508

Pump (P-73 / PM-308)

Function: To transfer buffer solution from storage tank to mixing tank

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Sodium Chloride	8.7342
	Tris Base	14.761
	WFI	3470.177
	Total	3493.672

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 840
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	Up to 133.33 LPM
	Tubing:	Bioprene, 40mm
	Sterilization:	SIP

<u>Operating Conditions:</u>	Pressure Change:	1 bar
	Pump Head:	44.1 ft
	Max. Flow Rate:	58.33 LPM
	Power Consumption:	0.14 kW

Purchase Cost: \$ 18,135

Reference Pages: 493, 505

Pump (P-74 / PM-309, P-75 / PM-310)

Function: To transfer buffer solution from storage tank to anion exchange chromatography column

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Sodium Chloride	1.0125
	Tris Base	1.7111
	WFI	402.279
	Total	405.0026

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	Up to 33.33 LPM
	Tubing:	Bioprene, 25 mm
	Sterilization:	SIP

<u>Operating Conditions:</u>	Pressure Change:	1 bar
	Pump Head:	44.1 ft
	Max. Flow Rate:	14.14 LPM
	Power Consumption:	0.075 hp

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Pump (P-76 / PM-311)

Function: To transfer buffer solution from storage tank to anion exchange chromatography column

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Sodium Chloride	26.11021
	Tris Base	2.23362
	WFI	446.79333
	Total	475.137

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	Up to 33.33 LPM
	Tubing:	Bioprene, 25 mm
	Sterilization:	SIP

<u>Operating Conditions:</u>	Pressure Change:	1 bar
	Pump Head:	44.1 ft
	Max. Flow Rate:	9.42 LPM
	Power Consumption:	0.0295 hp

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Storage Tank (P-77 / V-304)

Function: To mix and hold buffer solution for anion exchange chromatography

Vendor: Sharpsville Container

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Sodium Chloride	9.7467
	Tris Base	16.4719
	WFI	3872.4568
	Total	3899.19

<u>Characteristics:</u>	Material of Construction:	Stainless Steel 316L
	Total Volume:	4339.69 L
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25 °C
	Operating Pressure:	1 bar

Purchase Cost: \$117,000

Reference Page: 508

Storage Tank (P-78 / V-305)

Function: To mix and hold buffer solution for anion exchange chromatography

Vendor: Sharpsville Container

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Sodium Chloride	26.1102
	TRIS Base	2.2336
	WFI	446.7933
	Total	475.2

<u>Characteristics:</u>	<u>Material of Construction:</u>	Stainless Steel 316L
	Total Volume:	515.22 L
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25 °C
	Operating Pressure:	1 bar

Purchase Cost: \$ 117,000

Reference Page: 508

Pump (P-79 / PM-312)

Function: To transfer solution for to PEGylation section

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-09

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Impurities	0.00040
	MAB Fab Fragments	15.00984
	MES	0.53318
	Sodium Chloride	12.21593
	Tris Base	15.24966
	WFI	3800.25778
	Total	3843.267

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	Up to 33.33 LPM
	Tubing:	Bioprene, 25 mm
	Sterilization:	SIP

<u>Operating Conditions:</u>	Pressure Change:	1 bar
	Pump Head:	50.1 ft
	Max. Flow Rate:	16.04 LPM
	Power Consumption:	0.038 kW

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Diafiltration Storage Tank (P-80 / V-401)

Function: To store purified Fab fragments from Ion Exchange Chromatography prior to Diafiltration 1 process.

Vendor: Sharpsville Container

PFD Reference: PFD-10A

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
<u>Materials Handled:</u>	MAB Fab Fragments	15.01
	MES	0.53
	Sodium Chloride	12.22
	TRIS Base	15.25
	WFI	3800.26
	TOTAL (kg/batch)	3843.27

<u>Characteristics:</u>	Capacity:	4277.24 L
	Inside Diameter:	1.537 m
	Height:	2.305 m
	Interior Construction:	316L Electropolished Stainless Steel
	Sterilization:	SIP / CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Pressure:	22.04 psi

Purchase Cost: \$ 111,000

Reference Page: 508

Diafiltration Unit (P-81 / DF-401)

Function: To concentrate the Fab fragments from 3.9 mg/ml to 10 mg/ml in Reduction Reaction Buffer to prepare for the Reduction Reaction.

Vendor: Sartorius Stedim Biotechnology

PFD Reference: PFD-10A

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	EDTA, Sodium	5.69
	MAB Fab Fragments	15.01
	MES	0.53
	Phosphate	72.60
	Sodium Chloride	12.22
	TRIS Base	15.25
	WFI	12948.40
	TOTAL (kg/batch)	13069.70

<u>Characteristics:</u>	Cassette Model:	Sartocube® 302 144 59 30 E-BSW
	Membrane:	Hydrosart (stabilized cellulose based)
	Filter Area per Cassette:	3.0 m ²
	Filter holder:	Sartocon 3
	Maximum feed pressure:	58 psi (4 bar)
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Number of units:	15
	Total Filter area:	43.56 m ²
	Filter MWCO:	10 kDa
	Temp:	25 °C
	Pressure Change:	14.5 psi

Purchase Cost: Ultrafiltration Housing: \$ 11,141
Ultrafiltration Cartridges: \$ 125,610

Reference Pages: 514, 516, 518, 520

Pump (P-82 / PM-401)

Function: To transport the Fab fragments concentrated in the Reduction Reaction Buffer from Diafiltration Unit (P-81 / DF-401) to the Thiol Reduction Reactor (P-83 / R-401).

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
EDTA, Sodium	0.94
MAB Fab Fragments	15.01
MES	0.03
<u>Materials Handled:</u> Phosphate	11.95
Sodium Chloride	0.63
TRIS Base	0.79
WFI	1454.82
TOTAL (kg/batch)	1484.17

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 840
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	133.3 L/min
	Power:	2.2 hp / 3.0 kW
	Tubing:	Bioprene 40 mm
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	0.15 hp/ 0.12 kW
	Volumetric Throughput:	48.36 L/min
	Pressure Change	50 psi

Purchase Cost: \$18,135

Reference Pages: 493, 505

Thiol Reduction Reactor (P-83 / R-401)

Function: To reduce any thiols attached to the cysteine which will then be specifically PEGylated during the PEGylation Reaction.

Vendor: Abec

PFD Reference: PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	5593.00
EDTA, Sodium	0.94
MAB Fab Fragments	15.01
MES	0.03
Phosphate	11.95
Sodium Chloride	0.63
TRIS Base	0.79
WFI	1454.82
TOTAL (kg/batch)	7077.17

Materials Handled:

<u>Characteristics:</u>	Material of Construction:	316L Stainless Steel, Electropolished
	Mode of agitation	Backward curved impeller
	Mode of Drive:	Top mechanical agitation
	Mode of Control:	DCS control system
	Volume:	1673.93 L
	Height:	2.371 m
	Diameter	0.948 m
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	37°C
	Incubation Time:	90 minutes

Purchase Cost: \$ 511,000

Reference Page: 507

Pump (P-84 / PM-402)

Function: To transport the reduced Fab fragments in the Reduction Reaction Buffer from the Thiol Reduction Reactor (P-83 / R-401) to Diafiltration Unit (P-86 / DF-402).

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-10A

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
<u>Materials Handled:</u>	2-MEA	9.01
	EDTA, Sodium	0.94
	MAB Fab Fragments	0.75
	MES	0.03
	Phosphate	11.95
	Reduced MAB Fab Fragments	14.26
	Sodium Chloride	0.63
	TRIS Base	0.79
	WFI	1454.82
	TOTAL (kg/batch)	1493.17

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 840
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	133.3 L/min
	Power:	2.2 hp / 3.0 kW
	Tubing:	Bioprene 40 mm
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	0.16 hp/ 0.12 kW
	Volumetric Throughput:	49.11 L/min
	Pressure Change	14.5 psi

Purchase Cost: \$ 18,135

Reference Pages: 493, 505

Diafiltration Storage Tank (P-85 / V-402)

Function: To store reduced Fab fragments from Thiol Reduction Reaction prior to Diafiltration process.

Vendor: Sharpsville Container

PFD Reference: PFD-10A

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	2-MEA	9.01
	EDTA, Sodium	0.94
	MAb Fab Fragments	0.75
	MES	0.03
	Phosphate	11.95
	Reduced MAb Fab Fragments	14.26
	Sodium Chloride	0.63
	TRIS Base	0.79
	WFI	1454.82
	TOTAL (kg/batch)	1493.17

<u>Characteristics:</u>	Capacity:	1678.37 L
	Inside Diameter:	0.893 m
	Height:	2.679 m
	Interior Construction:	316L Electropolished Stainless Steel
	Sterilization:	SIP / CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Pressure:	22.046 bar

Purchase Cost: \$ 115,000

Reference Page: 508

Diafiltration Unit (P-86 / DF-402)

Function: To filter out 2-MEA and switch the reduced Fab fragments to PEGylation Reaction Buffer while maintaining a concentration of 10 mg/ml to prepare for the PEGylation Reaction.

Vendor: Sartorius Stedim Biotechnology

PFD Reference: PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	9.01
EDTA, Disodium	2.23
EDTA, Sodium	0.94
MAB Fab Fragments	0.75
MES	0.03
Phosphate	40.36
Reduced MAB Fab Fragments	14.26
Sodium Chloride	0.63
TRIS Base	0.79
WFI	4947.76
TOTAL (kg/batch)	5016.75

Materials Handled:

<u>Characteristics:</u>	Cassette Model:	Sartocube® 302 144 59 30 E-BSW
	Membrane:	Hydrosart (stabilized cellulose based)
	Filter Area per Cassette:	3.0 m ²
	Filter holder:	Sartocon 3
	Maximum feed pressure:	58 psi (4 bar)
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Number of units:	5
	Total Filter area:	13.03 m ²
	Filter MWCO:	10 kDa
	Temp:	25 °C
	Pressure Change:	152.68 psi

Purchase Cost: Ultrafiltration Housing: \$ 11,141
Ultrafiltration Cartridges: \$ 41,870

Reference Pages: 514, 516, 518, 520

Pump (P-87 / PM-403)

Function: To transport the reduced Fab fragments in the PEGylation Reaction Buffer from Diafiltration Unit (P-86 / DF-402) to the PEGylation Reactor (P-88 / R-402).

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-10A

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
<u>Materials Handled:</u>	2-MEA	1.22
	EDTA Disodium	0.95
	EDTA, Sodium	0.13
	MAB Fab Fragments	0.75
	Phosphate	13.78
	Reduced MAB Fab Fragments	14.26
	Sodium Chloride	0.09
	TRIS Base	0.11
	WFI	1477.31
	TOTAL (kg/batch)	1508.59

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 840
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	133.3 L/min
	Power:	2.2 hp / 3.0 kW
	Tubing:	Bioprene 40 mm
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	0.16 hp/ 0.12 kW
	Volumetric Throughput:	49.24 L/min
	Pressure Change	14.5 psi

Purchase Cost: \$ 18,135

Reference Pages: 493, 505

PEGylation Reactor (P-88 / R-402)

Function: To site-specifically PEGylate the 50 kDa Fab fragments with a 40 kDa PEG molecule to enhance therapeutic effects of the drug.

Vendor: Abec

PFD Reference: PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	1.22
EDTA, Disodium	0.95
EDTA, Sodium	0.13
MAb Fab Fragments	0.75
<u>Materials Handled:</u> Phosphate	13.78
Reduced MAb Fab Fragments	14.26
Sodium Chloride	0.09
TRIS Base	0.11
WFI	1477.31
PEG	228.15
TOTAL (kg/batch)	1745.59

<u>Characteristics:</u>	Material of Construction:	316L Stainless Steel, Electropolished
	Mode of agitation	Backward curved impeller
	Mode of Drive:	Top mechanical agitation
	Mode of Control:	DCS control system
	Volume:	1947.83 L
	Height:	2.493 m
	Diameter	0.997 m
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25°C
	Incubation Time:	120 minutes

Purchase Cost: \$ 522,000

Reference Page: 507

Pump (P-89 / PM-404)

Function: To transport the PEGylated Fab fragments, excess PEG molecules, and non-PEGylated Fab fragments in PEGylation Reaction Buffer from the PEGylation Reactor (P-88 / R-402) to Diafiltration Unit (P-91 / DF-403).

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	1.22
EDTA, Disodium	0.95
EDTA, Sodium	0.13
MAB Fab Fragments	0.75
PEG	217.31
<u>Materials Handled:</u> PEGylated MAb F	24.38
Phosphate	13.78
Reduced MAB Fab Fragments	0.71
Sodium Chloride	0.09
TRIS Base	0.11
WFI	590.92
TOTAL (kg/batch)	850.36

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Max Flow Rate:	33.3 L/min
	Max Power:	1.6 hp / 1.1 kW
	Tubing:	Bioprene 25 mm
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	0.09 hp/ 0.07 kW
	Volumetric Throughput:	27.84 L/min
	Pressure Change	14.5 psi

Purchase Cost: \$ 12,135

Reference Pages: 493, 505

Diafiltration Storage Tank (P-90 / V-403)

Function: To store PEGylated Fab fragments mixed with non-PEGylated Fab fragments and excess PEG molecules prior to Diafiltration process.

Vendor: Sharpsville Container

PFD Reference: PFD-10A

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	2-MEA	1.22
	EDTA, Disodium	0.95
	EDTA, Sodium	0.13
	MAB Fab Fragments	0.75
	PEG	217.31
<u>Materials Handled:</u>	PEGylated MAB F	24.38
	Phosphate	13.78
	Reduced MAB Fab Fragments	0.71
	Sodium Chloride	0.09
	TRIS Base	0.11
	WFI	590.92
	TOTAL (kg/batch)	850.36

<u>Characteristics:</u>	Capacity:	950.09 L
	Inside Diameter:	0.739 m
	Height:	2.216 m
	Interior Construction:	316L Electropolished Stainless Steel
	Sterilization:	SIP / CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Pressure:	26.1 psi

Purchase Cost: \$ 117,000

Reference Page: 508

Diafiltration Unit (P-91 / DF-403)

Function:	To switch the PEGylated Fab fragments, non-PEGylated Fab fragments, and excess PEG molecules from PEGylation Reaction Buffer to WFI while maintaining a concentration of 10 mg/ml to prepare for the cation exchange chromatography.
Vendor:	Sartorius Stedim Biotechnology
PFD Reference:	PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	1.22
EDTA, Disodium	0.95
EDTA, Sodium	0.13
MAb Fab Fragments	0.75
PEG	217.31
PEGylated MAb F	24.38
Phosphate	13.78
Reduced MAb Fab Fragments	0.71
Sodium Chloride	0.09
TRIS Base	0.11
WFI	2812.17
TOTAL (kg/batch)	3071.61

<u>Characteristics:</u>	Cassette Model:	Sartocube® 302 144 59 30 E-BSW
	Membrane:	Hydrosart (stabilized cellulose based)
	Filter Area per Cassette:	3.0 m ²
	Filter holder:	Sartocon 3
	Maximum feed pressure:	58 psi (4 bar)
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Number of units:	3
	Total Filter area:	7.39 m ²
	Filter MWCO:	30 kDa
	Temp:	25 °C
	Pressure Change:	26.1 psi

Purchase Cost: Ultrafiltration Housing: \$ 11,141
Ultrafiltration Cartridges: \$ 25,122 / 3m²

Reference Page: 514, 516, 518, 520

Cation Buffer 2 Storage Tank (P-92 / V-405)

Function: To store Cation Buffer 1 for Cation Exchange Chromatography Elution and Stripping steps.

Vendor: Sharpsville Container

PFD Reference: PFD-10A

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Phosphate	3.48
	Sodium Chloride	107.26
	WFI	1833.58
	TOTAL (kg/batch)	1944.33

<u>Characteristics:</u>	Capacity:	2113.64 L
	Inside Diameter:	0.96 m
	Height:	2.89 m
	Interior Construction:	316L Electropolished Stainless Steel
	Sterilization:	SIP / CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Pressure:	132.23 psi

Purchase Cost: \$ 119,000

Reference Page: 508

Cation Buffer 1 Storage Tank (P-93 / V-404)

Function: To store Cation Buffer 2 for Cation Exchange Chromatography
Equilibration, Wash, and Load steps.

Vendor: Sharpsville Container

PFD Reference: PFD-10A

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
<u>Materials Handled:</u>	Phosphate	6.87
	WFI	3618.45
	TOTAL (kg/batch)	3625.32

<u>Characteristics:</u>	Capacity:	4049.58 L
	Inside Diameter:	1.198 m
	Height:	3.594 m
	Interior Construction:	316L Electropolished Stainless Steel
	Sterilization:	SIP / CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Pressure:	132.23 psi

Purchase Cost: \$ 109,000

Reference Page: 508

Pump (P-94 / PM-405)

Function: To transport the PEGylated Fab fragments, excess PEG molecules, and non-PEGylated Fab fragments in WFI from Diafiltration Unit (P-91 / DF-403) to Cation Exchange Chromatography (P-101 / C-401).

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	0.17
EDTA, Disodium	0.13
EDTA, Sodium	0.02
MAb Fab Fragments	0.10
PEG	29.41
PEGylated MAb F	24.38
<u>Materials Handled:</u> Phosphate	1.87
Reduced MAb Fab Fragments	0.10
Sodium Chloride	0.01
TRIS Base	0.01
WFI	802.27
TOTAL (kg/batch)	858.47

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 840
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	133.3 L/min
	Power:	2.2 hp / 3.0 kW
	Tubing:	Bioprene 40 mm
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	0.16 hp/ 0.12 kW
	Volumetric Throughput:	48.79 L/min
	Pressure Change	14.5 psi

Purchase Cost: \$18,135

Reference Pages: 493, 505

Pump (P-95 / PM-406)

Function: To transport Cation Buffer 1 from the Storage Tank (P-93 / V-404) to Cation Exchange Chromatography (P-101 / C-401) for the loading step after mixing with the main Fab stream.

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-10A

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
<u>Materials Handled:</u>	Phosphate	3.96
	WFI	2084.92
	TOTAL (kg/batch)	2088.88

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 840
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	133.3 L/min
	Power:	2.2 hp / 3.0 kW
	Tubing:	Bioprene 40 mm
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	0.38 hp/ 0.29 kW
	Volumetric Throughput:	119.83 L/min
	Pressure Change	14.5 psi

Purchase Cost: \$18,135

Reference Pages: 493, 505

Pump (P-96 / PM-410)

Function: To transport Cation Buffer 2 from the Storage Tank (P-92 / V-405) to Cation Exchange Chromatography (P-101 / C-401) for the Stripping step.

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-10A

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Phosphate	1.41
	Sodium Chloride	43.55
	WFI	744.42
	TOTAL (kg/batch)	789.38

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Max Flow Rate:	33.3 L/min
	Max Power:	1.6 hp / 1.1 kW
	Tubing:	Bioprene 25 mm
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	0.08 hp/ 0.06 kW
	Volumetric Throughput:	25.18 L/min
	Pressure Change	14.5 psi

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Pump (P-97 / PM-411)

Function: To transport Cation Buffer 2 from the Storage Tank (P-92 / V-405) to Cation Exchange Chromatography (P-101 / C-401) for the Elution step.

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-10A

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Phosphate	2.07
	Sodium Chloride	63.72
	WFI	1089.16
	TOTAL (kg/batch)	1154.94

<u>Characteristics:</u>	Model: Pump Type: Material of Construction: Max Flow Rate: Max Power: Tubing: Sterilization:	Watson-Marlow Bredel 825 Peristaltic Stainless Steel 316L 33.3 L/min 1.6 hp / 1.1 kW Bioprene 25 mm SIP/CIP
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<u>Operating Conditions:</u>	Temp: Power: Volumetric Throughput: Pressure Change	25 °C 0.03 hp/ 0.02 kW 9.21 L/min 14.5 psi
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Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Pump (P-98 / PM-408)

Function: To transport Cation Buffer 1 from the Storage Tank (P-93 / V-404) to Cation Exchange Chromatography (P-101 / C-401) for the Wash step.

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-10A

Operation: Batch

<u>Input:</u>	<u>Quantity (kg/batch):</u>
2-MEA	0.17
EDTA, Disodium	0.13
EDTA, Sodium	0.02
MAb Fab Fragments	0.10
PEG	29.41
PEGylated MAb F	24.38
Phosphate	1.87
Reduced MAb Fab Fragments	0.10
Sodium Chloride	0.01
TRIS Base	0.01
WFI	802.27
TOTAL (kg/batch)	858.47

Materials Handled:

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Max Flow Rate:	33.3 L/min
	Max Power:	1.6 hp / 1.1 kW
	Tubing:	Bioprene 25 mm
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	0.06 hp/ 0.04 kW
	Volumetric Throughput:	18.88 L/min
	Pressure Change	14.5 psi

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Pump (P-99 / PM-407)

Function: To transport Cation Buffer 1 from the Storage Tank (P-93 / V-404) to Cation Exchange Chromatography (P-101 / C-401) for the Equilibration step.

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-10A

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
<u>Materials Handled:</u>	Phosphate	1.46
	WFI	766.76
	TOTAL (kg/batch)	768.22

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Max Flow Rate:	33.3 L/min
	Max Power:	1.6 hp / 1.1 kW
	Tubing:	Bioprene 25 mm
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Power:	0.08 hp/ 0.06 kW
	Volumetric Throughput:	25.18 L/min
	Pressure Change	14.5 psi

Purchase Cost: \$12,350

Reference Pages: 493, 505

Ion Exchange Chromatography (P-101 / C-401)

Function: To specifically bind and elute the PEGylated Fab' fragments in Cation Buffer 2.

Vendor: GE Amersham

PFD Reference: PFD-10A

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	2-MEA	0.17
	EDTA, Disodium	0.13
	EDTA, Sodium	0.02
	MAB Fab Fragments	0.10
	PEG	29.41
	PEGylated MAb F	24.38
	Phosphate	5.83
	Reduced MAB Fab Fragments	0.10
	Sodium Chloride	0.01
	TRIS Base	0.01
	Water	2084.92
	WFI	802.27
	TOTAL (kg/batch)	2947.35

<u>Characteristics:</u>	Model:	Chromaflow 1000
	Material of Construction:	Stainless Steel 316L
	Column Volume:	617.85 L
	Column Height:	0.787 m
	Column Diameter:	1.0 m
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temp:	25 °C
	Bed Volume:	154.46 L
	Resin:	MacroCap SP
	Binding Capacity:	150 mg/ml

Purchase Cost: Column: \$ 249,000
MacroCap SP Resin: \$ 290,230

Reference Page: 529

Pump (P-102 / PM-501)

Function: To transfer solution from to PEGylation to diafiltration

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-11

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Impurities	0.00001
	MAB Fab Fragments	0.00025
	PEGylated MAB Fab Fragments	22.00609
	Phosphate	0.27583
	Sodium Chloride	8.49544
	WFI	302.64578
	Total	333.423

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	Up to 33.33 LPM
	Tubing:	Bioprene, 25 mm
	Sterilization:	SIP

<u>Operating Conditions:</u>	Pressure Change:	1 bar
	Pump Head:	45.9
	Max. Flow Rate:	5.52 LPM
	Power Consumption:	0.005 kW

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Diafiltration Storage Tank (P-103 / V-501)

Function: To store product containing stream prior to diafiltration

Vendor: Sharpsville Container

PFD Reference: PFD-11

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Impurities	0.00001
	MAB Fab Fragments	0.00025
	PEGylated MAB Fab Fragments	22.0061
	Phosphate	0.2758
	Sodium Chloride	8.4954
	WFI	302.6458
	Total	333.4668

<u>Characteristics:</u>	Material of Construction:	Stainless Steel 316L
	Total Volume:	367.82 L
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Temperature:	25 °C
	Operating Pressure:	1 bar

Purchase Cost: \$ 117,000

Reference Page: 508

Diafiltration Unit (P-104 / DF-501)

Function: To concentrate monoclonal antibody stream and exchange buffer solution to PBS

Vendor: Sartorius Stedim Biotechnology

PFD Reference: PFD-11

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	Impurities	0.00001
	MAB Fab Fragments	0.00025
	PBS	440.95913
	PEGylated MAB Fab Fragments	22.0061
	Phosphate	0.2758
	Sodium Chloride	8.4954
	WFI	800.000
	Total	1271.73

<u>Characteristics:</u>	Cassette Model:	Sartocube® 302 144 59 30 E-BSW
	Membrane:	Hydrosart (stabilized cellulose based)
	Filter Area per Cassette:	3.0 m ²
	Filter holder:	Sartocon 3
	Maximum feed pressure:	58 psi (4 bar)
	Sterilization:	SIP/CIP

<u>Operating Conditions:</u>	Number of units:	1
	Total Filter area:	2.759 m ²
	Filter MWCO:	30 kDa
	Temperature:	25 °C

Purchase Cost: Ultrafiltration Housing: \$ 11,141

Ultrafiltration Cartridge: \$ 8374 / 3m²

Reference Page: 514, 516, 518, 520

Pump (P-105 / PM-502)

Function: To transfer solution from diafiltration to viral filtration

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-11

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
<u>Materials Handled:</u>	KCl	0.00034
	KH ₂ PO ₄	0.00034
	MAB Fab Fragments	0.00025
	Na ₂ HPO ₄	0.18291
	PEGylated MAB Fab Fragments	21.45594
	Phosphate	0.02402
	Sodium Chloride	2.11584
	WFI	196.844
	Total	220.360

<u>Characteristics:</u>	Model:	Watson-Marlow Bredel 825
	Pump Type:	Peristaltic
	Material of Construction:	Stainless Steel 316L
	Flow Rate:	Up to 33.33 LPM
	Tubing:	Bioprene, 25 mm
	Sterilization:	SIP

<u>Operating Conditions:</u>	Pump Head:	50.1 ft
	Max. Flow Rate:	3.68 LPM
	Power Consumption:	0.036 kW

Purchase Cost: \$ 12,350

Reference Pages: 493, 505

Retrovirus Filter (P-106 / DE-501)

Function: Removal of retrovirus from the monoclonal antibody stream

Vendor: Millipore

PFD Reference: PFD-11

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	KCl	0.00034
	KH ₂ PO ₄	0.00034
	MAB Fab Fragments	0.00025
	Na ₂ HPO ₄	0.18291
	PEGylated MAB Fab Fragments	21.45594
	Phosphate	0.02402
	Sodium Chloride	2.11584
	WFI	196.844
	Total	220.360

<u>Characteristics:</u>	Filter Model:	Viresolve NFR Cartridge Filter (10in)
	Filtration Area:	0.43 m ²
	Filter Material:	Polyethersulfone
	Filter Size Cutoff:	50 nm
	Process Volume:	600-1200L

<u>Operating Conditions:</u>	Temperature:	25°C
	Filtration Mode:	Normal Flow Filtration (Dead-End)

<u>Purchase Cost:</u>	Filter: \$1,459
	Housing \$1,340

Parvovirus Filter (P-107 / DE-502)

Function: Removal of parvovirus from the monoclonal antibody stream

Vendor: Millipore

PFD Reference: PFD-11

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
<u>Materials Handled:</u>	KCl	0.00034
	KH ₂ PO ₄	0.00034
	MAB Fab Fragments	0.00025
	Na ₂ HPO ₄	0.18900
	PEGylated MAB Fab Fragments	21.24138
	Phosphate	0.02399
	Sodium Chloride	2.11355
	WFI	196.63112
	Total	220.200

<u>Characteristics:</u>	Filter Model:	Viresolve NFP Cartridge Filter (10in)
	Filtration Area:	0.42 m ²
	Filter Material:	Modified PVDF
	Filter Size Cutoff:	20 nm
	Process Volume:	250L

<u>Operating Conditions:</u>	Temperature:	25°C
	Filtration Mode:	Normal Flow Filtration (Dead-End)

<u>Purchase Cost:</u>	Filter: \$3,963
	Housing: \$1,340

Bag Dispenser (P-108 / DCS-501)

Function: To transfer solution into 50 L bags

Vendor: SciLog, HyClone

PFD Reference: PFD-11

Operation: Batch

	<u>Input:</u>	<u>Quantity (kg/batch):</u>
<u>Materials Handled:</u>	Impurities	0.0000
	KCl	0.0003
	KH ₂ PO ₄	0.0003
	MAb Fab Fragments	0.0002
	Na ₂ HPO ₄	0.1888
	PEGylated MAb F	21.0290
	Phosphate	0.0240
	Sodium Chloride	2.1113
	WFI	196.4200
	Total	221.0122

<u>Characteristics:</u>	Dispenser Model:	SciLog Fillmaster 104B
	Pump Type:	Peristaltic
	Max Flow Rate:	14.6 L/min
	Sterilization:	SIP/CIP

Bag Material:	HyQ CX5-14 Film
Sterilization:	Pre-sterilized

Operating Conditions: Temperature: 25°C

<u>Purchase Cost:</u>	Dispensing Pump Unit:	\$10,000
	Five 50L Sterile Bags:	\$245.05

Reference Page: 541

Ultra Cold Freezer (P-109 / EC-501)

Function: To transfer solution for to PEGylation section

Vendor: Watson-Marlow Bredel

PFD Reference: PFD-11

Operation: Batch

<u>Materials Handled:</u>	<u>Input:</u>	<u>Quantity (kg/batch):</u>
	KCl	0.00034
	KH ₂ PO ₄	0.00034
	MAb Fab Fragments	0.00025
	Na ₂ HPO ₄	0.18880
	PEGylated MAb F	21.02897
	Phosphate	0.02397
	Sodium Chloride	2.11128
	WFI	196.42002
	Total	219.774

<u>Characteristics:</u>	Model:	TF-1050
	Material of Construction:	Stainless Steel 304
	Temperature Range:	-20°C to -85°C
	Size	1050 L

<u>Operating Conditions:</u>	Temperature:	-80°C
	Power Consumption:	10.85 kW

Purchase Cost: \$ 45,000

10.0 Cost Summary

10.1 Inoculum Prep and Bioreaction

Inoculum Prep - Bioreaction						
Name	Type	Units	Size (Capacity)		Material of Construction	Vendor Purchase Cost (\$/Unit)
TFR-101	T-Flask	20.00	4.50	L		Nunc \$6.83
RBR-101	Roller Bottle	11.00	24.20	L	CS	Nunc \$19.40
SBR-101	Seed Reactor	1.00	1439.60	L	SS316	ABEC \$495,000.00
MP-101	Blending Tank	1.00	952.15	L	SS316	Sharpsville Container \$117,000.00
DE-101	Sterile Filter Housing	1.00	10.00	m2	SS316	Sartorius Stedim Biotech \$1,908.00
	Filter Unit					Sartorius Stedim Biotech \$608.00
BBS-101	Disposable Bioreactor Skid	8.00	160.00	L	CS	Sartorius Stedim Biotech \$33,000.00
	Bag	8.00				Sartorius Stedim Biotech \$447.00
BBS-102	Disposable Bioreactor Skid	7.00	700.00	L	CS	Sartorius Stedim Biotech \$39,000.00
	Bag	7.00				\$447.00
MP-102	Blending Tank	1.00	2951.41	L	SS316	Sharpsville Container \$120,000.00
DE-102	Sterile Filter Housing	1.00	10.00	m2	SS316	Sartorius Stedim Biotech \$1,908.00
	Filter Unit					Sartorius Stedim Biotech \$608.00
SBR-102	Stirred Reactor	1.00	4455.30	L	SS316	ABEC \$585,000.00
MP-103	Blending Tank	1.00	7661.60	L	SS316	Sharpsville Container \$130,000.00
DE-103	Dead-End Filter Housing	1.00	10.00	m2	SS316	Sartorius Stedim Biotech \$1,908.00
	Filter					Sartorius Stedim Biotech \$608.00
MP-104	Blending Tank	1.00	1564.84	L	SS316	Sharpsville Container \$117,000.00
DE-104	Dead-End Filter Housing	1.00	10.00	m2	SS316	Sartorius Stedim Biotech \$1,908.00
	Filter					Sartorius Stedim Biotech \$608.00
PBR-101	Stirred Reactor	2.00	14062.54	L	SS316	ABEC \$661,000.00
PM-101	Pump	1.00	0.05	kW	SS316	Watson Marlow \$12,500.00
PM-102	Pump	1.00	0.05	kW	SS316	Watson Marlow \$12,500.00
PM-103	Pump	1.00	0.04	kW	SS316	Watson Marlow \$12,500.00
PM-104	Pump	1.00	0.08	kW	SS316	Watson Marlow \$12,500.00
PM-105	Pump	1.00	0.08	kW	SS316	Watson Marlow \$12,500.00
PM-106	Pump	1.00	0.02	kW	SS316	Watson Marlow \$12,500.00
PM-107	Pump	1.00	0.21	kW	SS316	Watson Marlow \$12,500.00
PM-108	Pump	1.00	0.21	kW	SS316	Watson Marlow \$12,500.00
PM-109	Pump	1.00	0.04	kW	SS316	Watson Marlow \$12,500.00
PM-110	Pump	1.00	0.04	kW	SS316	Watson Marlow \$12,500.00

10.2 Primary Recovery – Disulfide Reduction

Primary Recovery - Disulfide Reduction							
Name	Type	Units	Size (Capacity)		Material of Construction	Vendor	Purchase Cost (\$/Unit)
V-201	Blending Tank	1.00	10889.01	L	SS316	Sharpsville Container	\$129,000.00
V-202	Blending Tank	1.00	9667.46	L	SS316	Sharpsville Container	\$117,000.00
DS-201	Disk-Stack Centrifuge	1.00	1800.01	L/h	SS316	Alfa-Laval	\$421,000.00
DE-201	Dead-End Filter Housing	1.00	10.00	m2	SS316	Sartorius Stedim Biotech	\$1,908.00
	Filter					Sartorius Stedim Biotech	\$608.00
PM-201	Pump	1.00	0.12	kW	SS316	Watson Marlow	\$12,500.00
PM-202	Pump	1.00	0.11	kW	SS316	Watson Marlow	\$12,500.00
PM-203	Pump	1.00	0.11	kW	SS316	Watson Marlow	\$12,500.00
PM-204	Pump	1.00	0.54	kW	SS316	Watson Marlow	\$12,500.00
V-203	Blending Tank	1.00	9667.52	L	SS316	Sharpsville Container	\$17,000.00
DF-201	Diafilter	2.00	14.90	m2	SS316	Sartorius Stedim Biotech	\$41,870.00
	Diafilter Housing					Sartorius Stedim Biotech	\$11,141.00
R-201	Stirred Reactor	1.00	8422.52	L	SS316	ABEC	\$639,000.00
PM-205	Pump	1.00	0.73	kW	SS316	Watson Marlow	\$12,500.00
PM-206	Pump	1.00	9.03	kW	SS316	Watson Marlow	\$12,500.00
PFF-201	Plate & Frame Filter	1.00	23.23	m2	SS316	Pall Corporation	\$74,000.00
PM-207	Pump	1.00	9.06	kW	SS316	Watson Marlow	\$12,500.00
V-204	Blending Tank	1.00	4708.01	L	SS316	Sharpsville Container	\$117,000.00
DF-202	Diafiltration Housing	1.00	36.45	m2	SS316	Sartorius Stedim Biotech	\$83,000.00
	Diafilter					Sartorius Stedim Biotech	
R-202	Stirred Reactor	1.00	4738.43	L	SS316	ABEC	\$590,000.00
PM-209	Pump	1.00	0.33	kW	SS316	Watson Marlow	\$18,135.00
PM-208	Pump	1.00	9.16	kW	SS316	Watson Marlow	\$18,135.00
V-205	Blending Tank	1.00	4760.28	L	SS316	Sharpsville Container	\$117,000.00
DF-203	Diafiltration Housing	1.00	36.45	m2	SS316	Sartorius Stedim Biotech	\$83,000.00
	Diafilter					Sartorius Stedim Biotech	

10.3 Protein A – Chemical Virus Inactivation

Protein A - Chemical Virus Inactivation							
Name	Type	Units	Size (Capacity)		Material of Construction	Vendor	Purchase Cost (\$/Unit)
DE-202	Sterile Filter Housing	1.00	---	---	SS316	Sartorius Stedim	\$1,908.00
	Filter	1 / batch	1.80	m2	Polyethersulfone	Sartorius Stedim	\$608.00
V-206	Blending Tank	1.00	4797.72	L	SS316	Sharpsville Container	\$117,000.00
DF-204	Diafiltration Housing	6.00	14.90	m2	SS316	Sartorius Stedim	\$49,000.00
	Diafiltration Cassettes	5 / housing	3	m2	stabilized cellulose based membrane	Sartorius Stedim	\$1,200.00
V-207	Blending Tank	1.00	963.24	L	SS316	Sharpsville Container	\$117,000.00
DE-203	Sterile Filter Housing	1.00	---	---	SS316	Sartorius Stedim	\$1,908.00
	Filter	1 / batch	1.80	m2	Polyethersulfone	Sartorius Stedim	\$608.00
PM-211	Pump	1.00	0.62	kW	SS316	Watson Marlow	\$12,500.00
PM-212	Pump	1.00	0.62	kW	SS316	Watson Marlow	\$12,500.00
PM-213	Pump	1.00	0.62	kW	SS316	Watson Marlow	\$12,500.00
PM-214	Pump	1.00	0.62	kW	SS316	Watson Marlow	\$12,500.00
C-201	PBA Chromatography Column	1.00	8.46	L	SS316	GE LifeSciences	\$121,000.00
	Chromatography Resin					GE LifeSciences	7000/L
PM-210	Pump	1.00	0.61	kW	SS316	Watson Marlow	\$12,500.00

10.4 Cation and Anion Exchange Chromatography

Cation and Anion Exchange Columns							
Name	Type	Units	Size (Capacity)		Material of Construction	Vendor	Purchase Cost (\$/Unit)
V-301	Blending Tank	1.00	11223.72	L	SS316- Electropolished	Sharpsville Container	\$125,000.00
V-302	Blending Tank	1.00	1070.05	L	SS316- Electropolished	Sharpsville Container	\$115,000.00
V-303	Blending Tank	1.00	4145.41	L	SS316- Electropolished	Sharpsville Container	\$120,000.00
V-304	Blending Tank	1.00	4339.69	L	SS316- Electropolished	Sharpsville Container	\$120,000.00
V-305	Blending Tank	1.00	515.22	L	SS316- Electropolished	Sharpsville Container	\$112,000.00
V-306	Blending Tank	1.00	4275.00	L	SS316- Electropolished	Sharpsville Container	\$120,000.00
C-301	Chrom. Column	1.00	431.83	L	PE/SS316	GE	\$245,000.00
C-302	Chrom. Column	1.00	141.37	L	PE/SS316	GE	\$177,000.00
	Cation Resin	1	110	L	Toyopearl Gigacap S-650M	Tosoh Bioscience	\$182,490.00
	Anion Resin	1	65	L	Toyopearl SuperQ-650M	Tosoh Bioscience	\$64,870.00
PM-301	Pump	1.00	0.01	kW	SS316- Electropolished	Watson-Marlow	\$12,500.00
PM-302	Pump	1.00	0.06	kW	SS316- Electropolished	Watson-Marlow	\$12,500.00
PM-303	Pump	1.00	0.06	kW	SS316- Electropolished	Watson-Marlow	\$12,500.00
PM-304	Pump	1.00	0.01	kW	SS316- Electropolished	Watson-Marlow	\$12,500.00
PM-306	Pump	1.00	0.11	kW	SS316- Electropolished	Watson-Marlow	\$12,500.00
PM-307	Pump	1.00	0.11	kW	SS316- Electropolished	Watson-Marlow	\$18,135.00
PM-308	Pump	1.00	0.14	kW	SS316- Electropolished	Watson-Marlow	\$18,135.00
PM-309	Pump	1.00	0.06	kW	SS316- Electropolished	Watson-Marlow	\$12,500.00
PM-310	Pump	1.00	0.05	kW	SS316- Electropolished	Watson-Marlow	\$12,500.00
PM-311	Pump	1.00	0.02	kW	SS316- Electropolished	Watson-Marlow	\$12,500.00
PM-312	Pump	1.00	0.01	kW	SS316- Electropolished	Watson-Marlow	\$12,500.00

10.5 PEGylation

PEGylation							
Name	Type	Units	Size (Capacity)		Material of Construction	Vendor	Purchase Cost (\$/Unit)
R-401	Stirred Reactor	1.00	1659.53	L	SS316	ABEC	\$511,000.00
R-402	Stirred Reactor	1.00	1930.30	L	SS316	ABEC	\$521,000.00
V-402	Blending Tank	1.00	1663.96	L	SS316	Sharpsville Container	\$117,000.00
DF-402	Diafilter	1.00	12.91	m2	SS316	Sartorius Stedim	\$45,000.00
V-401	Blending Tank	1.00	4240.52	L	SS316	Sharpsville Container	\$117,000.00
DF-401	Diafilter	3.00	14.40	m2	SS316	Sartorius Stedim	\$48,000.00
V-403	Blending Tank	1.00	945.09	L	SS316	Sharpsville Container	\$117,000.00
DF-403	Diafilter	1.00	7.34	m2	SS316	Sartorius Stedim	\$32,000.00
PM-401	Centrifugal Pump	1.00	0.11	kW	SS316	Watson Marlow	\$18,135.00
PM-402	Centrifugal Pump	1.00	0.12		SS316	Watson Marlow	\$18,135.00
PM-404	Centrifugal Pump	1.00	0.07	kW	SS316	Watson Marlow	\$12,500.00
PM-403	Centrifugal Pump	1.00	0.12		SS316	Watson Marlow	\$18,135.00
C-401	PBA Chromatography Column	1.00	530.42	L	SS316	GE Healthcare Life Sciences	\$121,000.00
	Chromatography Resin	1.00	154.46	L	MacroCap SP	GE LifeSciences	\$290,230.00
MX-102	Mixer	1.00	10059.40	kg/h	SS316		\$0.00
V-404	Blending Tank	1.00	3806.73		SS316	Sharpsville Container	\$117,000.00
V-405	Blending Tank	1.00	1814.55	L	SS316	Sharpsville Container	\$117,000.00
PM-407	Centrifugal Pump	1.00	0.05	kW	SS316	Watson Marlow	\$12,500.00
PM-408	Centrifugal Pump	1.00	0.04		SS316	Watson Marlow	\$12,500.00
PM-406	Centrifugal Pump	1.00	0.28	kW	SS316	Watson Marlow	\$18,135.00
PM-405	Centrifugal Pump	1.00	0.12		SS316	Watson Marlow	\$18,135.00
PM-411	Centrifugal Pump	1.00	0.02	kW	SS316	Watson Marlow	\$12,500.00
PM-410	Centrifugal Pump	1.00	0.05		SS316	Watson Marlow	\$12,500.00

10.6 Final Filtration

Final Filtration							
Name	Type	Units	Size (Capacity)		Material of Construction	Vendor	Purchase Cost (\$/Unit)
Extra Unit	Sterile Liquid Dis.	1				SciLog	\$10,000.00
Extra Unit	10 in. Filter Housing	1.00			SS316- Electropolished	Millipore	\$1,354.00
Extra Unit	10 in. Filter Housing	1.00			SS316- Electropolished	Millipore	\$1,354.00
	Diafilter Housing	1.00					\$11,141.00
V-501	Blending Tank	1.00	363.51	L	SS316- Electropolished	Sharpsville Container	\$12,000.00
PM-501	Centrifugal Pump	1.00	0.02	kW	SS316- Electropolished	Watson-Marlow	\$12,500.00
PM-502	Centrifugal Pump	1.00	0.04	kW	SS316- Electropolished	Watson-Marlow	\$12,500.00
EC-501	Refrigerator	1.00	1050.00	L		Cincinnati Sub Zero	\$45,000.00

10.7 Additional Equipment

Additional Equipment			
Type	Units	Vendor	Purchase Cost (\$/Unit)
Incubators	2	Thermo Scientific	\$15,000.00
Roller Bottle Apparatus	1	Cole-Parmer	\$6,500.00
Biosafety Cabinet	1	Thermo Scientific	\$10,000.00
HVAC Equipment	1	-	\$1,200,000.00
Clean Steam Generator	1	-	\$200,000.00
CIP Skids	3	Sani-matic	\$80,000.00
Buffer Transfer Bags	-	HyClone	\$70,000/year
Filter Integrity Tester	1	Millipore	\$16,500.00
Tube Fuser	1	Sartorius Stedim Biotech	\$15,300.00
Tube Sealer	1	Sartorius Stedim Biotech	\$10,200.00
Water Treatment Package	1	-	\$100,000.00
WFI Still	1	Paul Mueller Co.	\$350,000.00
Biowaste and Neutralization Waste Tanks	2	Sartorius Stedim Biotech	\$125,000.00
Biowaste Inactivation System	1	-	\$270,000.00
Waste Neutralization System	1	-	\$100,000.00
Blood Gas Analyzer	1	Nova Biomedical	\$45,000.00
LIMS		Starlims	\$450,000.00
Pump on Cart	1	Watson Marlow	\$12,500.00
Final Packaging	1	Quality BioResources, Inc.	\$270,000/batch

11.0 Other Important Considerations

11.1 Scheduling

The total amount of time that it takes for one batch of monoclonal antibodies to go through the longest option in this flexible manufacturing facility is 40 days. However, the slowest part of the process is the bioreaction section, in which the main production bioreactor has a procedure time of about 10 days. The downstream following the bioreactor, from primary recovery to final formulation, has a total process of time of about 5 days. Using two main production reactors, a new batch can be started about every 5 days, when the equipment upstream of the main production bioreactor becomes available as most units before the main reactor take about 4-5 days. By using two production bioreactors and slightly staggering the batches, the production efficiency of this process can be greatly increased over a process that only used one main production reactor (see figure 11.1). Not only does this result in significantly greater production capacity, it helps alleviate the problem of the entire downstream remaining unused for a large portion of the time.

The plant will be run for 330 days a year and 6 days will be allowed between batches to be sure that they are staggered sufficiently. This is done to account for cleaning and validation, any required maintenance, or other problems that may arise in such a sensitive process. According to this scheduling, the plant will be able to produce 55 batches of PEGylated monoclonal antibodies per year. Economic analysis was performed based on this production schedule.

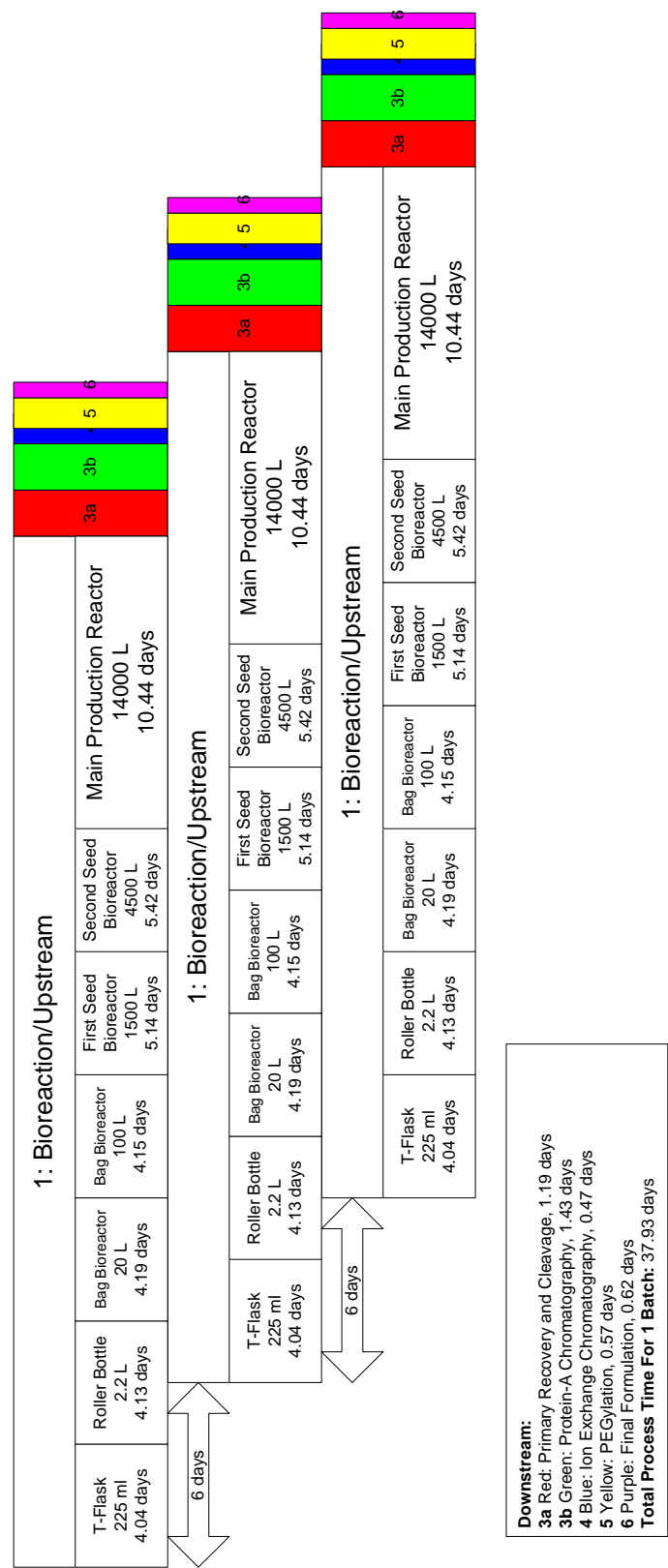


Figure 11.1 Gantt chart for entire process

11.2 Environmental Concerns

In the production of monoclonal antibodies, the main environmental concerns are those that deal with waste disposal. Both biological and non-biological waste is produced and must be disposed of properly. Biological waste can be found in the waste streams of the bioreactors and primary recovery, as they may contain living cells, either bacterial or mammalian, and viruses that are considered biohazards. These biological waste streams will be sent to and treated by the biowaste inactivation package, which will heat the waste to 80°C for 1 minute and inactivate the mammalian cell cultures. The biowaste is combined with all other non-biological waste in the waste neutralization tank, which adjusts the pH to 7.0, and then released into the sewage system. T-flasks, roller bottles, and the Wave bags will contain living cells as well, and must be autoclaved before disposal.

Plant emissions consist only of nitrogen, oxygen, and carbon dioxide, the major components of air. Although carbon dioxide emissions have come to be a large concern, emission from our plant is not deemed to be a considerable amount.

Another environmental concern is the waste generated through use of disposables. These disposable bags, flasks, and bottles contribute to a large amount of the waste generated by the facility. This is an environmental concern because there is limited landfill space and they are made of plastic and not biodegradable. Generally, these plastic disposables are not recycled. As disposables become more and more popular, recycling systems or services should become available.

11.3 Current Good Manufacturing Practices

Current Good Manufacturing Practices are enforced in the United States by the Food and Drug Administration (FDA). These guidelines ensure that drug products are safe and effective for human consumption, and therefore much care is needed to monitor the quality and sterility of them. In order to be assured of a product's quality, the manufacturer must pay careful attention to a number of factors. These include that only quality parts and materials are used to produce a certain drug, that the product and process have been adequately designed, that the layout of the plant is conducive to sterile production (See Section 11.4), that the process is controlled and monitored by operators at all times, and that a form of in-process and end-product testing is routine for each batch. Manufacturers must not rely on end-product testing alone since these tests may have limited sensitivity (FDA).

Sterility assurance measures are used to make sure that no contaminants of any kind have entered the product. This is accomplished by using standard CIP and SIP techniques following each batch for most pieces of equipment used. See the CIP and SIP section in Appendix A. Disposable bags for bioreactors, media, and buffers are helpful in maintaining a sterile process since their sterility is certified by their manufacturers. Sterile tube sealers and tube fusers also help to make sure that tube connections remain sterile.

Quality assurance requires that the product be tested throughout the process by quality control inspectors. Miniscule samples of the streams flowing out of a piece of equipment are tested in a quality control lab to ensure that each batch is producing a uniform product.

Proper process documentation including a validation protocol must be written and maintained for the manufacturer and for the FDA. This is a written plan stating how validation will be conducted, including test parameters, product characteristics, production equipment, and decision points on what constitutes acceptable test results. Each batch process must be written

and authenticated with operator signatures when performed in order to make sure that each batch is producing an identical product and to keep a paper trail in case there are issues that arise with the drug later on.

The diagram shown on the previous page is the layout of a typical biotechnology production facility similar to the flexible process for PEGylated monoclonal antibodies described herein. The FDA recommends that the layout of such a plant should mimic that of an assembly line, consisting of steps that are “in line” in one direction such that production begins on one side of the facility and ends on the other side. There is a clean corridor that allows traffic to flow to the left and return to the right. The general flow of materials in the diagram is right to left.

12.0 Economic Analysis

12.1 Market Analysis

According to the scheduling of our processes, as described in section 11.1, our facility is able to run a total of 55 batches per year, with each batch producing roughly 18 kg of our PEGylated monoclonal antibody. This results in the possibility to produce a total of 993 kg of product per year. However, the very competitive marketplace of biopharmaceuticals limits the potential market share of our product. This obstacle is overcome by the flexibility that is built into our manufacturing facility. Flexibility will allow for the production of various products each at amounts smaller than the maximum, thus allowing for profitability in the facility. The production capacity for the facility has nonetheless been estimated to be 75% of the design capacity in order to model the potential market share our facility will be able to capture from competing therapeutics.

In April 2008, Cimzia® (certolizumab pegol), an anti-TNF- α PEGylated Fab' fragment, was approved by the U.S. FDA for treatment of adult patients with moderate to severe Crohn's disease (Melmel, 2008). The current wholesale acquisition cost for Cimzia® is \$1,316 per 400 mg dose, administered every four weeks (Caremark®, 2008). According to Melmel et al, the projected first year sales for Cimzia® are \$50,000,000. Therefore, a simple calculation gives 3,166 patients in this first year and with each patient requiring 4.8 g per year, a yearly production amount of 15.2 kg/year is required. However, we predict that PEGylated mAb Fab' therapeutics, like Cimzia®, are likely to be approved for other indications including rheumatoid arthritis. This would lead to an increase in the yearly production amount, and may also increase the retail price for this therapeutic.

12.2 Profitability Analysis

The profitability analysis worksheet (Version 1.1), developed by Nickish Consulting, was used to determine the profitability of the processing plant. The following sections describe the relevant sections of this worksheet.

12.2.1 Price of PEGylated Monoclonal Antibody

While the PEGylation of the monoclonal antibody increases the price at which it should be sold to consumers, it also lowers the dosing requirements for this biopharmaceutical. Thus, instead of calculated consumer selling prices, the cost at which the product will be sold back to the client while maintaining profitability was determined. Competition in the market serves to drive down the price at which the facility can sell the product back to the client, and was taken into account for the pricing of our product. While the wholesale cost for Cimzia® is \$3,290,000 per kg, the retail cost can be assumed to be much more than this. Also, the flexibility of our facility will allow for the production of other antibodies, some which sell for as much as roughly \$25,000,000 per kg. Thus, a conservative estimate of \$5,000,000 per kg was used in profitability calculations.

12.2.2 Plant Life

The biopharmaceutical and bioprocess industries are continuously innovating and improving their products and processes. Patents may run out and competitive or superior treatments for the same disease may arise too. For these reasons, the plant life of many biopharmaceutical plants can vary, with a worst-case scenario of 5 years. However, this particular biopharmaceutical manufacturing facility is directly in line with the direction that the industry is taking. That is to say, that not only does this facility have the capability of producing PEGylated mAbs, but it is also flexible, allowing for the production of other mAbs. Therefore, a plant life of ten years has been used in economic calculations.

12.2.3 Raw Materials and Equipment Costs

The price of all raw materials and equipment units was gathered by direct contact with various vendors. The bare module factors for the equipment units were found in *Product and Process Design Principles*. Unfortunately, the profitability analysis worksheet has a maximum of 15 allowable entries per section, thus some raw materials and equipment units were lumped together in order to perform the necessary calculations. Also, additional costs for packaging and various process consumables were input into the “utilities” section.

12.2.4 Total Permanent Investment

The Total Permanent Investment accounts for the costs of site preparations, service facilities, contingencies and contractor fees, land and plant start up. The percentages used for profitability calculations were found in *Product and Process Design Principles*.

12.2.5 Working Capital

The working capital of a facility is defined as the current assets less the current liabilities. More specifically, it is the sum of the cash reserves, inventory, and accounts receivable minus the accounts payable. In most cases, 30 days of cash reserved, accounts receivable, and accounts payable is sufficient in calculations. For the inventory of raw materials, 30 days of most items was assumed. For costly raw materials, specifically polyethylene glycol, an inventory of 7 days was assumed. For weekly shipping of product, 7 days of inventory of product is accounted for in the working capital.

12.2.6 Utilities

The utility quantities were input into the worksheet as a ratio of utility to the product produced. These were calculated from the total utility requirements calculated in Section 5.

12.2.7 Other Variable Costs

These costs include the selling/transferring expenses, administrative expenses, and the management incentive compensation.

12.2.8 Fixed Costs

According to a suggestion by Dr. Tiffany Rau, the total number of operators needed per shift was assumed to be 16, each with direct wages and benefits totaling \$40.00/hr. The wages and benefits of maintenance, quality control, and technical assistants were also figured into the fixed costs. There are usually two maintenance personnel, two quality control experts on staff at any given time. The technical assistant category includes a small group of 2-3 engineers.

Operating overhead includes the general plant overhead, as well as the mechanical department services, employee relations department and business services. Once again, the percentages for these values were found in *Product and Process Design Principles*.

12.2.9 Depreciation

The MACRS Tax-Basis Depreciation for 5 years is used in this process. The percentages of Total Depreciable Capital for 5 years, starting at year 1 are as follows, 20%, 32%, 19.20%, 11.52%, 11.52%, 5.76% (Seider, 2004).

12.3 Input Summary

Input Summary

General Information

Process Title: Flexible Manufacturing Facility for Biopharmaceuticals
 Product: Anti-TNF-a PEGylated mAb
 Plant Site Location: Northeast
 Site Factor: 1.10
 Operating Hours per Year: 7,920
 Operating Days per Year: 330
 Operating Factor: 0.9041

Chronology

Year	Action	Distribution of Total	Distribution of Total	Production Capacity (%)	Percentage of Total
		Permanent Investment	Working Capital	of Design Capacity	Capital Investment for Depreciation
Start Year	2009 Design	0.0%	0.0%	0.0%	
	2010 Construction	100.0%	100.0%	0.0%	
	2011 Production			1.9%	20.0%
	2012 Production			38.4%	32.0%
	2013 Production			75.0%	19.2%
	2014 Production			75.0%	11.5%
	2015 Production			75.0%	11.5%
	2016 Production			75.0%	5.8%
	2017 Production			75.0%	
	2018 Production			75.0%	
End Year	2019 Production			75.0%	
	2020 Production			75.0%	

Product Information

The Process will yield:

a	0 kg of Anti-TNF-a PEGylated mAb per hour.
a	3 kg of Anti-TNF-a PEGylated mAb per day.
a	993 kg of Anti-TNF-a PEGylated mAb per year.

The Price per kg of Anti-TNF-a PEGylated mAb is: \$ 5,000,000

Raw Materials

Raw Material	Unit of Measure	Ratio to Product	Cost of Raw Material
2-MEA	kg	0.5028 kg per kg of Anti-TNF-a PEGylated mAb	\$136.0 per kg
Anion Buffers	kg	242.3 kg per kg of Anti-TNF-a PEGylated mAb	\$0.5380 per kg
Cation Buffers	kg	877.3 kg per kg of Anti-TNF-a PEGylated mAb	\$2.3700 per kg
H3PO4	kg	1,177.8 kg per kg of Anti-TNF-a PEGylated mAb	\$0.1430 per kg
NaOH (0.1M & 0.5M)	kg	913.4 kg per kg of Anti-TNF-a PEGylated mAb	\$0.2321 per kg
Pepsin (Immobilized)	kg	170.7 kg per kg of Anti-TNF-a PEGylated mAb	\$167.0 per kg
Polyethylene Glycol (PEG)	g	22,814.0 g per kg of Anti-TNF-a PEGylated mAb	\$120.0 per g
Polysorbate 80	kg	0.0049 kg per kg of Anti-TNF-a PEGylated mAb	\$1.8330 per kg
Protein A Buffers	kg	5.3176 kg per kg of Anti-TNF-a PEGylated mAb	\$0.5153 per kg
Reaction Buffers	kg	2,604.5 kg per kg of Anti-TNF-a PEGylated mAb	\$9.8810 per kg
Serum Free Media	kg	42.8176 kg per kg of Anti-TNF-a PEGylated mAb	\$1,749.9 per kg
NaH2PO4, NaCl, PBS	kg	77.1049 kg per kg of Anti-TNF-a PEGylated mAb	\$2.5638 per kg
Tris HCl (1M & 10mM), Tris Base	kg	142.1 kg per kg of Anti-TNF-a PEGylated mAb	\$0.0707 per kg
WFI	L	2,657.8 L per kg of Anti-TNF-a PEGylated mAb	\$0.1500 per L

Equipments Costs

<u>Fabricated Equipment</u>	<u>Purchase Cost</u>	<u>Bare Module Factor</u>	<u>Bare Module Cost</u>
Chromatography Columns (4)	\$ 861,000	1.1	\$ 947,100
Diafiltration Housings (7)	\$ 381,870	2.32	\$ 885,938
Diafiltration Cassettes (35)	\$ 286,090	1.1	\$ 314,699
Disposable Bag Bioreactor Systems (15)	\$ 537,000	1.1	\$ 590,700
Disposable Reactor Bags (825)	\$ 368,775	1.1	\$ 405,653
Plate and Frame Filter	\$ 74,000	1.4	\$ 103,600
Sterile Filter Housings (7)	\$ 13,356	2.32	\$ 30,986
Production Bioreactor (2)	\$ 1,322,000	4.16	\$ 5,499,520
T-Flasks (1100) + Roller Bottles (605)	\$ 19,249	1	\$ 19,249
Sterile Filters (385)	\$ 234,080	1.1	\$ 257,488
Stirred Reactors (6)	\$ 3,341,000	4.16	\$ 13,898,560
HVAC Equipment	\$ 1,200,000	1	\$ 1,200,000

<u>Process Machinery</u>	<u>Purchase Cost</u>	<u>Bare Module Factor</u>	<u>Bare Module Cost</u>
Centrifuge	\$ 421,000	2.03	\$ 854,630
Peristaltic Pump with Cart	\$ 3,100	3.3	\$ 10,230
Pump-825B/R (34)	\$ 419,900	3.3	\$ 1,385,670
Pump-840B/R (8)	\$ 145,080	3.3	\$ 478,764
Sterile Liquid Distributor	\$ 10,000	2.5	\$ 25,000
Media Prep Blending Tanks (4)	\$ 71,000	4.16	\$ 295,360
Virus Inactivation Tank	\$ 24,000	4.16	\$ 99,840
Clean Steam Generator	\$ 200,000	2	\$ 400,000
CIP Skids (3)	\$ 720,000	4	\$ 2,880,000
WFI Still	\$ 350,000	4	\$ 1,400,000
LIM System	\$ 450,000	1.1	\$ 495,000

<u>Spares</u>	<u>Purchase Cost</u>	<u>Bare Module Factor</u>	<u>Bare Module Cost</u>
Filter Integrity Tester	\$ 16,500	1	\$ 16,500
Sterile Tube Fuser	\$ 15,300	1	\$ 15,300
Sterile Tube Sealer	\$ 10,200	1	\$ 10,200
Water Treatment Package	\$ 100,000	1.1	\$ 110,000
Bioinactivation System	\$ 270,000	3.5	\$ 945,000
Waste Neutralization System	\$ 100,000	3	\$ 300,000
Autoclave	\$ 160,000	1.7	\$ 272,000
Blood Gas Analyzer	\$ 45,000	1.1	\$ 49,500
Portable Pump on Cart	\$ 12,500	3.3	\$ 41,250

<u>Storage</u>	<u>Purchase Cost</u>	<u>Bare Module Factor</u>	<u>Bare Module Cost</u>
Storage Tanks (18)	\$ 2,106,000	4.16	\$ 8,760,960
Refrigeration Units	\$ 45,000	2.05	\$ 92,250
Incubators (2)	\$ 15,000	1.74	\$ 26,100
Biosafety Cabinet	\$ 10,000	1.1	\$ 11,000
Biowaste/Neutralization Tank	\$ 50,000	4.16	\$ 208,000
Roller Bottle Aparatus	\$ 6,500	1.1	\$ 7,150

*Derived Bare Module Factor

Total Permanent Investment

Cost of Site Preparations: 5.0% of Total Bare Module Costs
 Cost of Service Facilities: 5.0% of Total Bare Module Costs
 Allocated Costs for utility plants and related facilities: \$0
 Cost of Contingencies and Contractor Fees: 18.0% of Direct Permanent Investment
 Cost of Land: 2.0% of Total Depreciable Capital
 Cost of Royalties: \$0
 Cost of Plant Start-Up: 10.0% of Total Depreciable Capital

Working Capital

Anti-TNF-a PEGylated mAb	a	Inventory: 7 Days	a	21.06 kg
2-MEA	a	Inventory: 30 Days	a	45.38 kg
Anion Buffers	a	Inventory: 30 Days	a	21,865.98 kg
Cation Buffers	a	Inventory: 30 Days	a	79,180.43 kg
H3PO4	a	Inventory: 30 Days	a	106,300.45 kg
NaOH (0.1M & 0.5M)	a	Inventory: 30 Days	a	82,434.84 kg
Pepsin (Immobilized)	a	Inventory: 30 Days	a	15,402.16 kg
Polyethylene Glycol (PEG)	a	Inventory: 7 Days	a	480,424.82 g
Polysorbate 80	a	Inventory: 90 Days	a	1.32 kg
Protein A Buffers	a	Inventory: 30 Days	a	479.91 kg
Reaction Buffers	a	Inventory: 30 Days	a	235,056.77 kg
Serum Free Media	a	Inventory: 30 Days	a	3,864.29 kg
NaH2PO4, NaCl, PBS	a	Inventory: 30 Days	a	6,958.72 kg
Tris HCl (1M & 10mM), Tris	a	Inventory: 30 Days	a	12,822.64 kg
Chromatography Resins (all	a	Inventory: 30 Days	a	2,972.30 L
Accounts Receivable	a	30 Days		
Cash Reserves	a	30 Days		
Accounts Payable	a	30 Days		

Utilities

Utility	Unit of Measure	Ratio to Product	Cost of Utility
Process Water	L	2,724.1 L per kg of Anti-TNF-a PEGylated	\$0.0005 per L
Electricity	kW-hr	1,244.5 kW-hr per kg of Anti-TNF-a PEGy	\$0.0800 per kW-hr
Process Consumables	unit	2.9358 unit per kg of Anti-TNF-a PEGylate	\$213.2 per unit
Lyophilization/Packaging	vials	2,500.0 vials per kg of Anti-TNF-a PEGyla	\$1.2000 per vials

Byproducts

- no Byproducts -

Other Variable Costs

General Expenses

Selling / Transfer Expenses: 3.00% of Sales
 Direct Research: 0.00% of Sales
 Allocated Research: 0.00% of Sales
 Administrative Expense: 2.00% of Sales
 Management Incentive Compensation: 1.25% of Sales

Fixed Costs

Operations

Operators per Shift: 16 (Assuming 16 Shifts)
Direct Wages and Benefits: \$40.00 per Operator Hour
Direct Salaries and Benefits: 15.00% of Direct Wages and Benefits
Operating Supplies and Services: 6.00% of Direct Wages and Benefits
Technical Assistance to Manufacturing: \$4,125.00 per year, for each Operator per Shift
Control Laboratory: \$7,525.00 per year, for each Operator per Shift

Maintenance

Wages and Benefits: 4.50% of Total Depreciable Capital
Salaries and Benefits: 25.00% of Maintenance Wages and Benefits
Materials and Services: 100.00% of Maintenance Wages and Benefits
Maintenance Overhead: 5.00% of Maintenance Wages and Benefits

Operating Overhead

General Plant Overhead: 7.10% of Maintenance and Operations Wages and Benefits
Mechanical Department Services: 2.40% of Maintenance and Operations Wages and Benefits
Employee Relations Department: 5.90% of Maintenance and Operations Wages and Benefits
Business Services: 7.40% of Maintenance and Operations Wages and Benefits

Property Taxes and Insurance

Property Taxes and Insurance: 2.00% of Total Depreciable Capital

Straight Line Depreciation

Direct Plant: 8.00% of Total Depreciable Capital, less 1.18 times the Allocated Costs for Utility Plants and Related Facilities
Allocated Plant: 6.00% of 1.18 times the Allocated Costs for Utility Plants and Related Facilities

Depletion Allowance

Annual Depletion Allowance: \$0.00

12.4 Profitability Analysis

There are several ways for estimating profitability, the easiest of which is Return on Investment (ROI). As described in *Product and Process Design Principles*, the ROI “is the annual interest rate made by the profits on the original investment” (Seider, 2004). This is the least accurate method for calculating profitability since it assumes straight line depreciation. The ROI for this process is 53.0%.

The second method for estimating profitability involves the Net Present Value (NPV), which “provides a quantitative measure for comparing the capital required for competing processes in current terms” (Seider, 2004). The NPV of the process is \$1,319,592,100 after a plant life of 10 years.

The third method used for estimating the profitability of this process is to use the Investor’s Rate of Return (IRR), which is the interest rate which gives a net present value of zero. The IRR for this facility has been calculated to be 33.51%. This high IRR, which is likely to be higher than the market interest rate, conveys the profitability of the process. The following pages contain the results of the profitability worksheet for a plant life of 10 years, a selling price of \$5,000,000 per kg, modeled with an annual production of 744.6 kg/year (75% of the design capacity of 992.75 kg/year) of PEGylated mAb Fab’ therapeutics.

12.4.1 Profitability Analysis Results

April, 2009

Profitability Measures

Flexible Manufacturing Facility for Biopharmaceuticals

The Investor's Rate of Return (IRR) for this Project is: **33.51%**

The Net Present Value (NPV) at 15% for this Project is: **\$1,319,592,100**

ROI Analysis (Third Production Year)

Annual Sales:	\$3,722,812,500
Annual Costs:	-\$2,689,125,700
Depreciation:	-\$4,500,700
Income Tax:	-\$380,798,900
Net Earnings:	\$652,887,900
Total Capital Investment:	<u>\$1,231,787,600</u>
ROI:	53.0%

Investment Summary

April, 2009

Flexible Manufacturing Facility for Biopharmaceuticals

Bare Module Costs

Fabricated Equipment

Chromatography Columns (4)	\$947,100
Diafiltration Housings (7)	\$885,900
Diafiltration Cassettes (35)	\$314,700
Disposable Bag Bioreactor Systems (15)	\$590,700
Disposable Reactor Bags (825)	\$405,700
Plate and Frame Filter	\$103,600
Sterile Filter Housings (7)	\$31,000
Production Bioreactor (2)	\$5,499,500
T-Flasks (1100) + Roller Bottles (605)	\$19,200
Sterile Filters (385)	\$257,500
Stirred Reactors (6)	\$13,898,600
HVAC Equipment	\$1,200,000
Total Fabricated Equipment: \$24,153,500	

Process Machinery

Centrifuge	\$854,600
Peristaltic Pump with Cart	\$10,200
Pump-825B/R (34)	\$1,385,700
Pump-840B/R (8)	\$478,800
Sterile Liquid Distributor	\$25,000
Media Prep Blending Tanks (4)	\$295,400
Virus Inactivation Tank	\$99,800
Clean Steam Generator	\$400,000
CIP Skids (3)	\$2,880,000
WFI Still	\$1,400,000
LIM System	\$495,000
Total Process Machinery: \$8,324,500	

Spares

Filter Integrity Tester	\$16,500
Sterile Tube Fuser	\$15,300
Sterile Tube Sealer	\$10,200
Water Treatment Package	\$110,000
Bioinactivation System	\$945,000
Waste Neutralization System	\$300,000
Autoclave	\$272,000
Blood Gas Analyzer	\$49,500
Portable Pump on Cart	\$41,250
Total Spares: \$1,759,800	

Storage

Storage Tanks (18)	\$8,761,000
Refrigeration Units	\$92,300
Incubators (2)	\$26,100
Biosafety Cabinet	\$11,000
Bio waste/Neutralization Tank	\$208,000
Roller Bottle Apparatus	\$7,200
Total Storage: \$9,105,500	

TOTAL

Total Bare Module Costs:

\$43,343,000

Direct Permanent Investment		
Cost of Site Preparation:	\$2,167,200	
Cost of Service Facilities:	\$2,167,200	
Allocated Costs for utility plants and related facilities	\$0	
Direct Permanent Investment:		\$47,677,000
Total Depreciable Capital		
Cost of Contingencies and Contractor Fees:	\$8,581,900	
Total Depreciable Capital:		\$56,259,000
Total Permanent Investment		
Cost of Land:	\$1,125,200	
Cost of Royalties:	\$0	
Cost of Plant Start-Up:	\$5,625,900	
Total Permanent Investment:		\$63,010,000
Working Capital		
Inventory		
Anti-TNF-a PEG:	a 0 kg	\$78,968,800
2-MEA	a 0 kg	\$4,600
Anion Buffers	a 16,000 kg	\$8,800
Cation Buffers	a 59,000 kg	\$140,700
H3PO4	a 80,000 kg	\$11,400
NaOH (0.1M & 0	a 62,000 kg	\$14,300
Pepsin (Immobilized)	a 12,000 kg	\$1,929,100
Polyethylene Gly	a 360,000 g	\$43,238,200
Polysorbate 80	a 0 kg	\$0
Protein A Buffers	a 0 kg	\$200
Reaction Buffers	a 176,000 kg	\$1,741,900
Serum Free Med	a 3,000 kg	\$5,071,700
NaH2PO4, NaCl	a 5,000 kg	\$13,400
Tris HCl (1M & 1	a 10,000 kg	\$700
WFI	a 0 L	\$0
Chromatography	a 2,000 L	\$25,225,900
Total Inventory:		\$156,369,900
Accounts Receivable:		\$451,250,000
Cash Reserves:		\$268,495,600
Accounts Payable:		\$292,662,100
Total Working Capital:		\$1,168,777,600
TOTAL CAPITAL INVESTMENT		\$1,231,787,600

Variable Cost Summary

April, 2009

Flexible Manufacturing Facility for Biopharmaceuticals

	Per kg Anti-TNF-a PEGylated mAb		TOTAL
Raw Materials			
2-MEA	\$68.38 per kg of Anti-TNF-a PEGylated mAb	\$67,900	
Anion Buffers	\$130.35 per kg of Anti-TNF-a PEGylated mAb	\$129,400	
Cation Buffers	\$2,079.31 per kg of Anti-TNF-a PEGylated mAb	\$2,064,200	
H3PO4	\$168.43 per kg of Anti-TNF-a PEGylated mAb	\$167,200	
NaOH (0.1M & 0.5M)	\$212.00 per kg of Anti-TNF-a PEGylated mAb	\$210,500	
Pepsin (Immobilized)	\$28,500.40 per kg of Anti-TNF-a PEGylated mAb	\$28,293,800	
Polyethylene Glycol (PEG)	\$2,737,680.00 per kg of Anti-TNF-a PEGylated mAb	\$2,717,831,800	
Polysorbate 80	\$0.01 per kg of Anti-TNF-a PEGylated mAb	\$0	
Protein A Buffers	\$2.74 per kg of Anti-TNF-a PEGylated mAb	\$2,700	
Reaction Buffers	\$25,735.13 per kg of Anti-TNF-a PEGylated mAb	\$25,548,600	
Serum Free Media	\$74,927.88 per kg of Anti-TNF-a PEGylated mAb	\$74,384,600	
NaH2PO4, NaCl, PBS	\$197.68 per kg of Anti-TNF-a PEGylated mAb	\$196,200	
Tris HCl (1M & 10mM), Tris Base	\$10.04 per kg of Anti-TNF-a PEGylated mAb	\$10,000	
WFI	\$398.68 per kg of Anti-TNF-a PEGylated mAb	\$395,800	
Chromatography Resins (all)	\$372,682.28 per kg of Anti-TNF-a PEGylated mAb	\$369,980,300	
Total Raw Materials:	\$3,242,793.31 per kg of Anti-TNF-a PEGylated mAb	\$3,219,283,100	\$3,219,283,100
Utilities			
Process Water	\$1.48 per kg of Anti-TNF-a PEGylated mAb	\$1,500	
Electricity	\$99.56 per kg of Anti-TNF-a PEGylated mAb	\$98,800	
Process Consumables	\$625.96 per kg of Anti-TNF-a PEGylated mAb	\$621,400	
Lyophilization/Packaging	\$3,000.00 per kg of Anti-TNF-a PEGylated mAb	\$2,978,300	
Total Raw Materials:	\$3,726.99 per kg of Anti-TNF-a PEGylated mAb	\$3,700,000	\$3,222,983,100
Byproducts			
General Expenses			
Selling / Transfer:	\$150,000.00 per kg of Anti-TNF-a PEGylated mAb	\$148,912,500	
Direct Research:	\$0.00 per kg of Anti-TNF-a PEGylated mAb	\$0	
Allocated Research:	\$0.00 per kg of Anti-TNF-a PEGylated mAb	\$0	
Administrative Expense:	\$100,000.00 per kg of Anti-TNF-a PEGylated mAb	\$99,275,000	
Management Incentives:	\$62,500.00 per kg of Anti-TNF-a PEGylated mAb	\$62,046,900	
Total Byproducts:	\$312,500.00 per kg of Anti-TNF-a PEGylated mAb	\$310,234,400	\$3,533,217,500
TOTAL	\$3,559,020.31 per kg of Anti-TNF-a PEGylated mAb	\$3,533,217,400	\$3,533,217,400

Fixed Cost Summary

April, 2009

Flexible Manufacturing Facility for Biopharmaceuticals

		TOTAL
<u>Operations</u>		
Direct Wages and Benefits:	\$21,299,200	
Direct Salaries and Benefits:	\$3,194,880	
Operating Supplies and Services:	\$1,277,952	
Technical Assistance to Manufacturing:	\$66,000	
Control Laboratory:	\$120,400	
Total Operations: \$25,958,432		\$25,958,432
<u>Maintenance</u>		
Wages and Benefits:	\$2,531,655	
Salaries and Benefits:	\$632,914	
Materials and Services:	\$2,531,655	
Maintenance Overhead:	\$126,583	
Total Maintenance: \$5,822,807		\$31,781,239
<u>Operating Overhead</u>		
General Plant Overhead:	\$1,963,764	
Mechanical Department Services:	\$663,808	
Employee Relations Department:	\$1,631,860	
Business Services:	\$2,046,740	
Total Operating Overhead: \$6,306,172		\$38,087,411
<u>Property Insurance and Taxes</u>		
Total Property Insurance and Taxes: \$1,125,180		\$39,212,591
TOTAL		\$39,212,591

Cash Flow Summary														
Flexible Manufacturing Facility for Biopharmaceuticals														
Year		Percentage of Design Capacity	Sales	Capital Costs	Working Capital	Variable Costs	Fixed Costs	Depreciation Allowance	Depletion Allowance	Taxable Income	Income Tax Costs	Net Earnings	Annual Cash Flow	Cumulative Net Present Value at 15.0%
2009		0.0%	Design	\$0	\$0								\$0	\$0
2010		0.0%	Construction	-\$63,010,000	-\$1,168,777,600								-\$1,231,787,600	-\$1,071,119,700
2011		1.9%	\$94,311,300			-\$67,131,100	-\$39,212,600	-\$11,251,800	\$0	-\$23,284,200	\$8,615,200	-\$14,669,000	-\$3,417,200	-\$1,073,703,600
2012		38.4%	\$1,906,080,000			-\$1,356,755,500	-\$39,212,600	-\$18,002,900	\$0	\$492,109,000	-\$182,080,300	\$310,028,700	\$328,031,600	-\$858,017,500
2013		75.0%	\$3,722,812,500			-\$2,649,913,100	-\$39,212,600	-\$10,801,700	\$0	\$1,022,885,100	-\$378,467,500	\$644,417,600	\$655,219,300	-\$483,393,700
2014		75.0%	\$3,722,812,500			-\$2,649,913,100	-\$39,212,600	-\$6,481,000	\$0	\$1,027,205,800	-\$380,066,100	\$647,139,700	\$653,620,700	-\$158,428,700
2015		75.0%	\$3,722,812,500			-\$2,649,913,100	-\$39,212,600	-\$6,481,000	\$0	\$1,027,205,800	-\$380,066,100	\$647,139,700	\$653,620,700	\$124,149,600
2016		75.0%	\$3,722,812,500			-\$2,649,913,100	-\$39,212,600	-\$3,240,500	\$0	\$1,030,446,300	-\$381,265,100	\$649,181,200	\$652,421,700	\$369,419,100
2017		75.0%	\$3,722,812,500			-\$2,649,913,100	-\$39,212,600		\$0	\$1,033,686,800	-\$382,464,100	\$651,222,700	\$651,222,700	\$582,305,000
2018		75.0%	\$3,722,812,500			-\$2,649,913,100	-\$39,212,600		\$0	\$1,033,686,800	-\$382,464,100	\$651,222,700	\$651,222,700	\$767,423,100
2019		75.0%	\$3,722,812,500			-\$2,649,913,100	-\$39,212,600		\$0	\$1,033,686,800	-\$382,464,100	\$651,222,700	\$651,222,700	\$928,395,400
2020		75.0%	\$3,722,812,500			-\$2,649,913,100	-\$39,212,600		\$0	\$1,033,686,800	-\$382,464,100	\$651,222,700	\$1,820,000,300	\$1,319,592,100

IRR Analysis - Single Variable

Flexible Manufacturing Facility for Biopharmaceuticals

April, 2009

Product Prices

Product Prices	\$4,250,000.00	\$4,375,000.00	\$4,500,000.00	\$4,625,000.00	\$4,750,000.00	\$4,875,000.00	\$5,000,000.00	\$5,125,000.00	\$5,250,000.00	\$5,375,000.00	\$5,500,000.00	\$5,625,000.00	\$5,750,000.00
IRR	19.75%	22.41%	24.90%	27.24%	29.45%	31.53%	33.51%	35.39%	37.18%	38.89%	40.53%	42.09%	43.60%

Variable Cost

Variable Cost	\$3,003,234.800	\$3,091,565.200	\$3,179,895.700	\$3,268,226.100	\$3,356,556.500	\$3,444,887.000	\$3,533,217.400	\$3,621,547.800	\$3,709,878.300	\$3,798,208.700	\$3,886,539.100	\$3,974,869.600	\$4,063,200.000
IRR	42.88%	41.40%	39.89%	38.35%	36.78%	35.17%	33.51%	31.82%	30.08%	28.28%	26.44%	24.54%	22.58%

Fixed Cost

Fixed Cost	\$33,330,700	\$34,311,000	\$35,291,300	\$36,271,600	\$37,252,000	\$38,232,300	\$39,212,600	\$40,192,900	\$41,173,200	\$42,153,500	\$43,133,900	\$44,114,200	\$45,094,500
IRR	33.75%	33.71%	33.67%	33.63%	33.59%	33.55%	33.51%	33.47%	33.43%	33.39%	33.35%	33.31%	33.27%

Initial Investment (TPI)

Initial Investment	\$53,558,500.0	\$55,133,800	\$56,709,000	\$58,284,300	\$59,859,500	\$61,434,800	\$63,010,000	\$64,585,300	\$66,160,500	\$67,735,800	\$69,311,000	\$70,886,300	\$72,461,500
IRR	33.72%	33.69%	33.65%	33.62%	33.58%	33.55%	33.51%	33.48%	33.44%	33.41%	33.37%	33.34%	33.30%

12.5 Sensitivity Analysis

Several factors affect the profitability of this facility. Namely, the selling price of the PEGylated monoclonal antibody, the duration of the plant life, and the expenses of resins and the PEG molecule are all important to examine.

12.5.1 Selling Price

In order to determine the effect of selling price on profitability, various selling prices of PEGylated monoclonal antibodies produced at full capacity were varied while keeping all other variables constant. As shown in Figure 12.1, a gradual increase in selling price increases the IRR non-linearly. Effects on NPV and ROI are also shown in the table on the following page. Note how changes in prices drastically affect the return on investment.

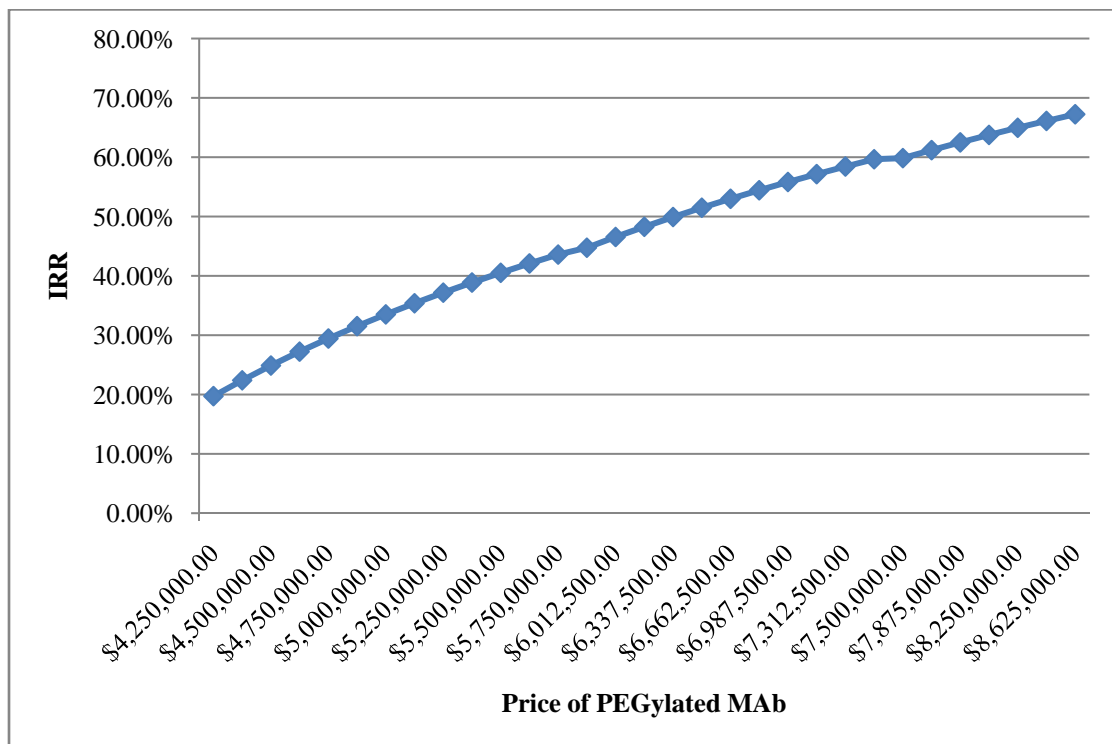


Figure 12.1: This is a single variable sensitivity analysis showing how changes in the selling price of the PEGylated monoclonal antibodies affects the IRR.

Product Price (\$MM)	IRR (%)	NPV (At 15%)	ROI (%)
6.50	51.5	\$3,396,412,000	94.4
6.25	49.05	\$3,050,275,500	88.1
6.00	46.43	\$2,704,138,500	81.7
5.50	40.53	\$2,011,865,400	67.9
5.00	33.51	\$1,319,592,100	53.0
4.50	24.90	\$627,318,800	36.7

Table 12.1 Selling price sensitivity analysis

12.5.2 Plant Life

The effect of plant life on profitability is can be seen in the table below. As plant life is increased from 5 to 15 years, IRR increases from 29.38% to 34.19%. NPV also increases and ranges from \$629.4 MM to \$1.66 billion.

Plant Life (years)	Selling Price (\$/gram)	IRR	NPV (At 15%)	ROI
5	\$5,000	29.38%	\$629,444,400	53%
7	\$5,000	32.03%	\$964,380,400	53%
10	\$5,000	33.51%	\$1,319,592,100	53%
15	\$5,000	34.19%	\$1,662,493,400	53%

Table 12.2 Plant life sensitivity analysis

12.5.3 Cost of Polyethylene Glycol

In order to determine the effect that the purchase cost for the raw material PEG has on profitability, various PEG prices were considered with production at full capacity while keeping all other variables constant. This was done because PEG is the most expensive raw material that is purchased for this process. Effects on IRR, NPV, and ROI are also shown in the following table. Note that significant decreases in the price of PEG greatly increase the IRR and ROI beyond reasonable expectations. In addition, significant increases in the price of PEG greatly decrease the IRR and ROI beyond the point where the facility would be profitable.

% Inc/Dec	Price of PEG (\$/g)	IRR (%)	NPV (At 15%)	ROI (%)
-50	60	64.96	\$3,610,659,700	132.8
-20	96	45.89	\$2,236,019,000	80.6
0	120	33.51	\$1,319,592,100	53.0
20	144	20.82	\$403,164,900	29.7

Table 12.3 Cost of polyethylene glycol sensitivity analysis

12.5.4 Cost of Chromatography Resins

The table below shows the effect of changing the cost of chromatography resins on the profitability of the process over 10 years. With the current calculated cost of resin, the IRR is 33.51%, the NPV is \$1,319,592,100, and the ROI is 53%. As the price of resin increases by 50%, the IRR drops 4.5 percent, the NPV decreases by more than \$300 million, and the ROI drops by 9%. On the other hand, as the price of resin decreases by 50%, the IRR increases to 37.96%, the NPV increases to \$1.637 billion, and the ROI rise to 62.4%. The cost of the chromatography resins has a strong impact on the profitability of the monoclonal antibody. Fortunately, the price of these resins should only decrease over time, as newer resins with higher binding capacities will enter the market.

Resin Cost Increase	Resin Cost (\$/L)	IRR	NPV (At 15%)	ROI
-50%	\$5,658	37.96%	\$1,637,807,000	62.4%
-20%	\$9,053	35.29%	\$1,440,866,700	56.7%
0	\$11,316	33.51%	\$1,319,592,100	53.0%
20%	\$13,579	31.74%	\$1,192,317,500	49.4%
50%	\$16,974	29.08%	\$1,001,377,300	44.3%

Table 12.4 Cost of chromatography resins sensitivity analysis

13.0 Conclusions and Recommendations

This report provides a detailed analysis of the production of PEGylated mAb Fab' therapeutics, as well as the production of various other biopharmaceutical products. If this facility were to be run at full capacity (for 330 days) with production bioreactors that yield 3.5 g/L titers, it would be able to produce 993 kg of PEGylated monoclonal antibodies. From economic analysis of this facility, it has been determined that a conservative selling price for PEGylated monoclonal antibodies would be \$5,000/g. Under the assumption that we would be running at 1.9% of this design capacity for the first year and increase to 75% over two years, the profitability analysis shows an NPV of \$1,319,592,100, an IRR of 33.51%, and a 53.0% ROI after three years. This design scheme was based on financial research of sales projections for the new therapeutic Cimzia® for its first year of production.

The flexibility of this facility will allow for the production of other biopharmaceutical monoclonal antibodies. Small biotech firms are currently producing 81 mAbs and many are looking to license production for their Phase III molecules. Thus, CMO's such as ours are working to capture much of this demand. Many of the mAbs generated by this facility will be able to yield great profit, especially since most, if not all, of the process equipment can be used to meet the demands of multiple products. It is for these reasons that we recommend that this facility be built, to not only meet the demands of the innovative PEGylated monoclonal antibody, but also a number of other biopharmaceuticals.

14.0 Acknowledgements

This design project could not have been completed without the combined efforts and expertise of many individuals. Firstly, we would like to thank Dr. Tiffany Rau, our industrial consultant who also drafted this design project. Dr. Rau went above and beyond what was expected of her as our consultant by taking valuable time out of her schedule to meet with us one weekend for several hours and help us with SuperPro Designer. She also took time to teleconference with us numerous times throughout the semester when any questions arose that we could not find the answers. She spent extra time at the University of Pennsylvania following design meetings when she was not meeting with our group in order to check in with us and offer advice. She emailed us frequently also during the week to help motivate us and provide helpful suggestions. She sent us many useful references which we used to complete the design. Overall, Dr. Rau was an invaluable resource and we were lucky to have her as we completed our project.

We would also like to thank our faculty advisor, Dr. Matthew Lazzara, for meeting with us and advising us throughout the semester. He sent us useful patent information on PEGylation as well as helped us with understanding the biological aspects of our process and why we were using certain pieces of equipment. He also suggested that we validate calculations made by SuperPro in order to ensure we were obtaining reasonable results and in order to learn how each unit operated.

Next, we would like to thank Professor Leonard Fabiano for helping us with some of our engineering calculations and for contacting CDI Corporation to help us with SuperPro and scheduling. Professor Fabiano also helped secure an updated version of SuperPro that was on the CETS network so that our group and other groups could benefit from the new features of the program.

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*Indicates PEGylation literature.

Appendix A – Calculations

Growth Rate

$$\text{Time required to double} = t_D = \frac{\ln 2}{m_{net}}$$

μ_{net} = net specific growth rate (h^{-1}) $\equiv \frac{1}{X} \frac{dX}{dt}$, where X is the cell mass concentration (gL^{-1})
(Sauer 2000)

for CHO cells: $\tau_D = 14\text{-}17$ hours

$$\therefore m_{net} = 0.04077\text{--}0.04951 \text{ hr}^{-1}$$

Growth Curves

The cells grown up in the batch inoculum and seed bioreaction sections of the process typically proceed through various phases. These include a lag phase, exponential phase, stationary phase, and lastly a death phase.

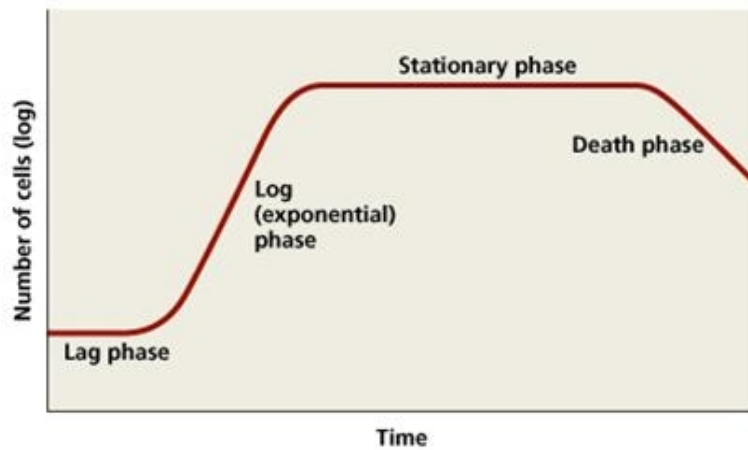


Figure A.1: This is a typical graph of the viable cell number versus time. Each phase of cell growth is labeled.

During the short-lived lag phase, cells in culture experience very little growth since they must adjust to their new environment. After this initial adjustment period, cells begin to actively divide themselves, leading into the exponential phase of growth. During this phase, the cell number increases exponentially with time. However, after a certain period of time, the cells use up all of their food and resources (namely glucose, vitamins, amino acids, and other nutrients from the serum free media) and growth slows down. This is considered to be the stationary phase. The number of cells that die is roughly equal to the number of cells that are created. Once a majority of the nutrients in the surrounding environment are used up, the cells move into the death phase. The cells in this phase have greater death rates than reproduction rates, so the number of viable cells decreases. If no new nutrients are added to the batch at this point, all the cells will eventually die.

For the batch reactors in this process, mammalian cells follow a similar growth curve. The lag phase generally lasts from 1-2 days. The exponential phase occurs anywhere from 2-3 days after inoculation and lasts about 1.5 days. This is the period of time at which monoclonal antibody production is at its highest. Therefore, it is of interest to lengthen the period of time at which cells growth is in the exponential phase. This is generally done by setting the bioreactor to fed batch mode which has been implemented for the production bioreactor in this process. For this mode, the lag phase generally lasts the same amount of time as in batch mode, but the exponential phase is extended from anywhere between 3-5 days. Additional feeding at regular intervals allows the cells to continue dividing and producing monoclonal antibodies since nutrients are constantly being replenished. Despite this additional feeding, the accumulation of toxic waste products begins to decrease the viability of the cells. The stationary phase is short-lived and only lasts for at the most 1 day until the death phase begins.

For this process, it has been determined that for each batch process bioreactor will operate for 4 days, while the fed batch bioreactor will operate for 9 days in order to maximize growth and production of monoclonal antibodies.

Antibody Production Rate

$$q_{Ab}^{ave} = \frac{(Ab_{t_{final}} \cdot V_{t_{final}} - Ab_{t_{initial}} \cdot V_{t_{initial}})}{\int_{t_{initial}}^{t_{final}} X_V V dt},$$

where Ab_t is the antibody concentration at time t , and $X_V V$ is the total number of viable cells (Sauer 2000)

According to Kumar et. al, productivities today are ~90 pg/cell/day.

Media Calculation

$$\text{Volume of the feed medium} = V_{\text{feed}} = \left(\frac{glc_{tar} - glc}{glc_{feed} - glc_{tar}} \right) \cdot V,$$

where glc_{tar} is the post-feed target glucose concentration, glc is the pre-feed glucose concentration, and glc_{feed} is the medium's glucose concentration.

$$\text{For a medium of 1:1: } glc_{feed} = \frac{1}{2}(1g/L) + (1.802g/L) = 1.401g/L$$

$$glc_{tar} = 4.5 g/L \text{ (time of feed addition is 30 minutes).}$$

Ammonia Levels

For CHO cells, there was found to be 50% growth reduction at 8 mM ammonium, PEGylation effects by levels of ammonium between 3 to 9 mM, and observed dependence on the extracellular pH.

CHO Cell Data

Dry Cell Weight: 390 pg/cell

$$\text{Oxygen Uptake Rate (OUR)} = k_{La} (C^* - C_R) + D(C_F - C_R)$$

k_{La} = liquid phase mass transfer coefficient for oxygen

C^* = liquid phase concentration of oxygen at equilibrium with the gas phase

C_R = concentration of oxygen in the liquid phase of the reactor

D = dilution rate

C_F = concentration of oxygen in the liquid feed

$$\text{Carbon dioxide Evolution Rate (CER)} = (n_g/V_R) (y_{CO_2}^R - y_{CO_2}^F) + D(C_A^R - C_A^F) \text{ (Nyberg 1999)}$$

Calculation of Product Amount

Calculations using Cimzia® (certolizumab pegol) for current sales projections:

$$\$1,316 \text{ per dose} \times 12 \text{ doses per patient per year} = \$15,792 \text{ per patient per year}$$

$$\frac{\text{First years sales}}{\text{Yearly cost for treatment}} = \frac{\$50,000,000}{\$15,792 \text{ per patient}} \rightarrow 3166 \text{ current patients/year}$$

$$\frac{\text{cost per dose}}{\text{kg per dose}} = \frac{\$1316}{400 \text{ mg}} \times \frac{1000 \text{ mg}}{\text{g}} \times \frac{1000 \text{ g}}{\text{kg}} = \$3,290,000 \text{ per kg}$$

$$\frac{400 \text{ mg}}{\text{dose}} \times \frac{12 \text{ doses}}{\text{year}} = 4.8 \text{ g per patient per year}$$

$$3166 \text{ patients} \times 4.8 \text{ g per patient per year} = 15,196.8 \text{ g} = 15.1968 \text{ kg}$$

A 25% increase in production for the first year:

$$15.1968 \text{ kg} \times 1.25 = 18.996 \text{ kg}$$

$$\frac{\text{Production amount in first year}}{\text{Annual design capacity of facility}} = \frac{18.996 \text{ kg}}{992.75 \text{ kg}} = 1.91\%$$

Calculations using Humira® (adalimumab) as a basis for future sales projections:

$$\frac{\text{Sales of Humira}}{\text{Cost per Patient/year}} = \frac{\$3.0 \times 10^9}{\$13,000} = 230,769 \text{ Patients/year}$$

$$\frac{230,769 \text{ patients}}{\text{year}} \times \frac{4.8 \text{ g}}{\text{patient/year}} = 1,107,690 \text{ g} \rightarrow 1,107.69 \text{ kg}$$

Vessel Sizing

SuperPro Designer was useful for sizing all of the vessels for this process, but as a validation the following equation was used on one of the bioreactors (“Reactor Considerations,” 1997)

Let:

D = diameter of the vessel (ft)

WV = working volume in the tank (gal)

F = fraction of total volume occupied by working volume

a = factor for determining the capacity in gallons of the bottom head = 0.606 for ASME Standard F & D heads

d = 5.875 gal/ft³

R = aspect ratio = L/D = 2.5

Then:

$$D = \left[\frac{(WF/F)}{a + dR} \right]^{1/3}$$

Example (PBR-101):

WV = 14,000 L = 3,698 gal

F = 0.7

a = 0.606

d = 5.875 gal/ft³

R = 2.5

$$D = \left[\frac{\left(3698 \text{ gal} / 0.7 \right)}{0.606 + 5.875 \frac{\text{gal}}{\text{ft}^3} * 2.5} \right]^{1/3} = 7.02 \text{ ft} = 2.1 \text{ m}$$

Note that this within 5% of the Superpro calculation of 2.0 m.

Stoichiometry of the Batch and Fed-Batch Bioreactors

A stoichiometric reaction for each batch bioreactor and for the fed-batch production bioreactor is used to model cell growth and monoclonal antibody production for this process. Note that for a more detailed analysis, a list of kinetically defined reactions detailing growth, maintenance, production, and death could have been used. However, it was determined that this single stoichiometric reaction listed below would provide a sufficient estimate for the growth of cells and production of monoclonal antibodies throughout the process.

REACTANTS		PRODUCTS	
Components	Mass Coeff %	Components	Mass Coeff%
Amino Acids	6.21	Biomass	34.26
Glucose	26.28	Carb. Dioxide	69.41
Glutamine	3.04	Dead Biomass	3.51
Inorganic Salts	63.66	MAB	7.03
Other Media	0.55	Water	61.5
Oxygen	100	Lactate	24.29
Vitamins	0.26		
Total	200		200

For the reactants side of the equation, 100 mass percent of serum free media is reacting with 100 mass percent of oxygen. The percentages of amino acids, glucose, glutamine, inorganic salts, other inactive components of the media, and vitamins are determined based on the percentage of each in the purchased media from Sigma-Aldrich and sum to 100 mass percent. Even though in reality the cells would not consume inorganic salts and the other inactive components of the media, these components are modeled in the equation for simplicity and assumed to convert into dead biomass and other impurities. The main purpose of the inorganic

salts is to control the pH of the media to about 7.2. This combined with the buffers will provide an effective environment for cell growth.

For the product side of the equation, the total components are out of 200 mass percent in order to properly balance the equation. First, the percentage of lactate was determined. Glucose from the reactants goes to lactate via a 1:1 mole ratio. Therefore, a mass conversion using the molecular weights of each component gives a percentage of lactate in the products that is slightly less than that of glucose in the reactants. The remaining percentages of biomass, carbon dioxide, dead biomass, monoclonal antibodies, and water were based on a monoclonal antibody production example provided by Intelligen employee Dr. Demetri Petrides which used the equation for the bioreactors:

REACTANTS		PRODUCTS	
Components	Mass Coeff %	Components	Mass Coeff %
Oxygen	100	Biomass	39
Serum Free Media	100	Carb. Dioxide	79
		Impurities	4
		MAB	8
		Water	70

The percentages of these products were thus adjusted to include lactate to give the equation shown on the previous page.

Clean-in-Place (CIP) and Steam-in-Place (SIP) Procedures

CIP and SIP procedures are used in the manufacturing process to remove biologically active contaminants such as cells from all process units after each batch.

The following CIP procedure will be used for all pipes, valves, and mixing tanks used throughout the process:

1. Each vessel will be washed with an amount of sterile water equal to half its volume for 10 minutes.
2. Next, a cleaning solution of caustic (NaOH 0.5 M) equal to half the vessel's volume will be sprayed into the tank for 30 minutes.
3. Sterile water will then be used as in step 1 to wash away the cleaning solution for 10 minutes.
4. Next, a cleaning solution of acid (H₃PO₄ 5% w/w) equal to half the vessel's volume will be sprayed into the tank for 30 minutes.
5. Sterile water will then be used as in step 1 to wash away the cleaning solution for 10 minutes.
6. Lastly, another half volume of sterile water will be used to wash the vessel once more before the next batch for 10 minutes.

This washing regime will use approximately 2 vessel volumes of water. This includes the water to be used to make the sterile wash solution.

CIP Calculations were performed by SuperPro Designer based on modified equations listed in (Stewart 1996) in which each vessel is sprayed in a certain number of bursts:

Let:

C = circumference of tank (ft)

V_t = total volume used (gal)

V_w = total water used (gal)

V_{caustic} = total concentrated caustic used (gal)

V_{acid} = total concentrated acid used (gal)

Then:

$$V_t = \frac{2.5 \text{ gal}}{\text{min} * \text{ft}} \times \frac{1.5 \text{ min}}{\text{burst} * \text{step}} \times 3 \text{ bursts} \times 5 \text{ steps} \times C$$

$$V_w = \frac{3}{5} V_t + \frac{2}{5} (99.5\% \times V_t)$$

$$V_{caustic} = V_{acid} = 0.5\% \times \frac{1}{5} V_t$$

For filter units such as diafiltration and ultrafiltration, the cleaning procedure determined by the manufacturers is as follows:

1. Flush each unit with sterile water at 50°C.
2. Circulate for one hour sodium hypochlorite (NaOCl) at 50°C with a pH around 10 or 11.
3. Repeat step 1.

A procedure including steam-in-place is necessary for large, less sensitive equipment such as the bioreactors and final storage tanks. Therefore the procedure will be changed as follows:

1. Each reactor will be washed with an amount of sterile water equal to half its volume for 10 minutes.
2. Next, a cleaning solution of caustic (NaOH 0.5 M) equal to half the vessel's volume will be sprayed into the vessel for 30 minutes.
3. Sterile water will then be used as in step 1 to wash away the cleaning solution.
4. Next, a cleaning solution of acid (H₃PO₄ 5% w/w) equal to half the vessel's volume will be sprayed into the tank for 30 minutes.
5. Sterile water will then be used as in step 1 to wash away the cleaning solution for 10 minutes.
6. 5 lb/hr of pure steam per cubic foot of vessel volume will be pumped into the vessel to heat it up to the temperature of the steam, 130°C. Note: The steam used in this procedure will be generated by a sterile steam generator at 130°C and 2 bars.
7. Once the 130°C has been reached in the vessel, the steam flow rate will be reduced to 1 lb/hr of pure steam per cubic foot of vessel volume and held at the flow rate for thirty minutes.
8. Lastly, after thirty minutes, the flow rate of steam will be stopped and a half volume of sterile water will then be sprayed into the tank to wash it and cool it down to room temperature. (Burbano 2001)

SIP calculations are also performed by Superpro Designer and are calculated with modified equations such as these:

Let:

V = volume of vessel or pump (ft³)

S_t = total steam required (lb)

S_c = volume of steam when condensed (L)

Then:

$$S_t = V \times \left[\left(\frac{5 \text{ lb}}{\text{hr} * \text{ft}^3} \times \frac{1}{60} \text{ hr} \right) + \left(\frac{1 \text{ lb}}{\text{hr} * \text{ft}^3} \times \frac{1}{2} \text{ hr} \right) \right]$$

$$S_c = S_t \times \left(\frac{\text{ft}^3}{62.4 \text{ lb}} \right) \left(\frac{28.31 \text{ L}}{\text{ft}^3} \right)$$

Appendix B – PEGylation

PEGylation Overview

Polyethylene glycol (PEG) is used often in the pharmaceutical industry to improve the pharmacokinetic effects of protein therapies (Knudson 2008). Attaching PEG(s) to protein products has helped to solve the dilemma of the short half-lives of proteins and peptides, since these products are removed from the body so quickly through dialysis in the kidneys. Not only does PEG conjugation increase retention time of a drug by slowing filtration in the kidneys, but it also helps protect against enzyme digestion of the drug and allows for less frequent injections for patients (Fishburn 2007).

While papain can be used to efficiently cleave Fab fragments that will not be PEGylated, it was found that pepsin cleavage to produce Fab' fragments is the better alternative for proteins that will be PEGylated. Therefore, this option was added to the process so that PEGylation can be done more efficiently. If the enzyme is not PEGylated, the enzyme papain is used since it requires fewer steps than pepsin cleavage and is the most efficient way to produce Fab fragments. Cleaving the mAbs with the enzyme pepsin requires extra reduction steps, but this is what allows for the high-efficiency, site-specific PEGylation. Traditionally, strong thiols were used to activate the disulphide bonds between the heavy and light chains of the Fab fragment and then these activated bonds were PEGylated. However, this non-specific PEGylation method results in a heterogeneous mixture of conjugates, some with loss of functionality and some PEGylated an undesirable number of times or on less optimal bond(s) (Brocchini 2006). Processes were developed to separate the mono-PEGylated Fabs and determine which locations were best to PEGylate. For Fab, the optimal PEGylation is mono-PEGylation furthest from the active end, which targets TNF- α , in order to avoid steric hindrance and maintain full function of

therapeutic effects. This requires additional steps to separate out the desired molecule, resulting in significant loss of Fab (Humphreys 2007).

To avoid these complications, methods have been discovered to site-specifically PEGylate. While there are ways to distinctively PEGylate the disulphide bonds in the Fab fragments themselves, this is difficult and breaking these bonds can alter the therapeutic effects of the protein (Brocchini 2006). For this reason, pepsin is used to cleave off fragments from the Fc region that consists of both Fabs linked by the hinge disulphide bonds, referred to as $F(ab')_2$ (See Figure 2.3). Reduction of these species produces two Fab' fragments, which are Fab fragments that retain a cysteine from the heavy-chain linking disulfide bonds in the hinge region. The thiol in this cysteine can then easily be PEGylated at high efficiency under mild conditions, allowing for site-specific PEGylation without interrupting the structure of the protein (Humphreys 2007) (See Figure 2.4). Mild reduction of the hinge region disulfide bonds is performed with a thiol-based compound which will only break the inter-heavy chain disulphide bonds and leave the disulphide bonds between the light and heavy chains of the Fab fragments intact (See Figure B.1). We cannot use stronger reducing agents or PEGylate on the disulfide bonds between the heavy and light chains of the Fab fragment as this would result in a decrease or loss of therapeutic effects of the protein.

In this process, Thermo Scientific's 2-Mercaptoethylamine·HCl (2-MEA) is used for the reduction. This 2-MEA compound is used again later in the process, right before PEGylation, as a mild reductant is again required to remove any small thiol-reactive molecules that cap the thiol that needs to be PEGylated, which can accumulate during purification steps (Humphreys 2007).

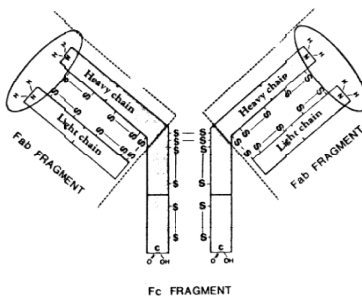


Figure B.1

Pepsin Cleavage and Disulphide Reduction Protocol and Calculations

Using Thermo Scientific/Pierce Immobilized Pepsin, the Mab will be cleaved right before the hinge region to form Fc fragments and F(ab')₂ molecules that consist of two Fabs held together by disulphide bonds in the hinge region of the Mab. These F(ab')₂ fragments will then be reduced with Thermo Scientific/Pierce 2-Mercaptoethylamine·HCl.

1. Diafiltration (P-35, DF-201) is performed to concentrate the Mab in Pepsin Digestion Buffer from a concentration of 3.56 mg/ml to 10 mg/ml. Buffer calculations are based on the amount of Mab in the incoming stream.

Pepsin Digestion Buffer	Mass (g/batch)	Mass Fraction	Mass %
NaOAc (2.72 g/L)	23666.10065	0.002712619	0.271262
HCl (To pH 4.5)	10.02894699	1.14952E-06	0.000115
WFI	8700772.298	0.997286232	99.72862
Total	8724448.427		

2. For the pepsin cleavage reaction, 0.5 ml Immobilized Pepsin previously equilibrated in Pepsin Digestion Buffer is added to the reactor per 1 ml Mab Solution in Digestion Buffer as per the Pierce protocol for Immobilized Pepsin Cleavage. This reaction mixture is incubated for 5 hours at 37°C with agitation. Using the Immobilized Pepsin in a 50% slurry, 5 ml settled gel has enough pepsin for 200 mg Mab.

3. Plate and Filter Filtration (P-39/PFF-201) removes suspended Immobilized Pepsin from the slurry.
4. Diafiltration (P-42/DF-202) is performed to remove any very small Fc fragments and concentrates the $F(ab')_2$ in Reduction Reaction Buffer from a concentration of 3.68 mg/mL to 10 mg/mL. Buffer calculations are based on the amount of $F(ab')_2$ in the incoming stream.

Reduction Reaction Buffer	Mass (g/batch)	Mass Fraction	Mass %
Phosphate (0.1 M, pH 6.0)	12667.57	0.8448176	84.48176
EDTA (2 mM)	993.0246	0.0662262	6.622616
Water	1333.85	0.0889563	8.895626
Total	14994.45		

5. The Disulphide Reduction Reaction (P-44/R-202) will produce 2 Fab' fragments from each $F(ab')_2$ molecule. As per the protocol for using Thermo Scientific's 2-Mercaptoethylamine-HCl, 6 mg of 2-MEA per mL of Fab' solution at 10 mg/ml is added to give 50 mM 2-MEA Solution. This is incubates for 90 minutes at 37°C, and then returned to room temperature (25°C).
6. Diafiltration (P-47/DF-203) is performed to separate out 2-MEA (114 Da) and exchange the Reduction Reaction Buffer with WFI while maintaining a concentration of 10 mg/ml for the Protein-A Chromatography which will specifically bind the Fab' fragments and purify them further.

PEGylation Protocol and Calculations

For the PEGylation Reaction, the Fab' fragments must first be reduced with Thermo Scientific/Pierce 2-Mercaptoethylamine-HCl, a mild reductant which will remove any thiols which became attached to the cysteine to be PEGylated during previous purification steps (Humphreys 2007). Then the fragments are PEGylated with JenKem USA's branched, thiol-

reactive 40 kDa PEG maleimide molecule, following the protocol used in Humphreys for PEGylation on Fab' fragments.

1. Diafiltration (P-81/DF-401) is performed to concentrate the Fab' fragments in Reduction Reaction Buffer from 3.9 mg/ml to 10 mg/ml. Calculations are based on the amount of Fab' in the incoming stream.

Reduction Reaction Buffer	Mass (g/batch)	Mass Fraction	Mass %
Phosphate (0.1 M, pH 6.0)	14254.85	0.009401	0.940072
EDTA (2 mM)	1117.453	0.000737	0.073693
Water	1500984	0.989862	98.98623
Total	1516356		

2. The Thiol Reduction Reaction (P-83/R-401) will prepare the cysteine for PEGylation. As per the protocol for using Thermo Scientific's 2-Mercaptoethylamine·HCl, 6 mg of 2-MEA per mL of Fab' solution at 10 mg/ml is added to give 50 mM 2-MEA Solution. This is incubates for 90 minutes at 37°C, and then returned to 25°C.
3. Diafiltration (P-86/DF-402) is performed to separate out 2-MEA (114 Da) and keep Reduced Fab' fragments at a concentration 10 mg/mL, though now in PEGylation Reaction Buffer. The 2-MEA protocol requires a buffer with a concentration of EDTA between 1 and 10 mM, so the Reduction Reaction Buffer used is the same PEGylation Reaction Buffer used for the PEGylation protocol in Humphreys. Calculations are based on the amount of Reduced Fab' in the incoming stream.

PEGylation Reaction Buffer	Mass	Mass Fraction	Mass %
NaOAc (2.72 g/L)	13542.1	0.009401	0.940072
HCl (To pH 4.5)	1061.58	0.000737	0.073693
WFI	1425935	0.989862	98.98623
Total	1440539		

4. As per the protocol followed by Humphreys, PEG is added to Fab' Solution and incubated at room temperature ($\sim 24^{\circ}\text{C}$) for 2 hours. An excess of 2 moles of PEG are added per mole of Fab' to ensure that the reaction goes to completion.
5. Diafiltration (P-91/DF-403) is conducted to switch the PEG Reaction Buffer with WFI for Cation Exchange Chromatography. A filter with a 30 kDa cutoff pore size is used to filter out excess PEG molecules (40 kDa) and non-PEGylated Fab' fragments (40 kDa) while retaining the PEGylated proteins (90 kDa) in the retentate.
6. Cation Exchange Chromatography (P-101/C-101) is performed to specifically isolate PEGylated Fab fragments. Buffer calculations are based on the provided protocol for using the GE Healthcare MacroCap SP resin.

Cation Buffer 1	Mass	Mass Fraction	Mass %
Phosphate (0.02 M, pH 6.8)	1.8994	0.001896	0.189579912
Water	1000	0.998104	99.81042009
Total	1001.899		
Cation Buffer 2	Mass	Mass Fraction	Mass %
Phosphate (0.02 M, pH 6.8)	1.8994	0.001791	0.179129634
NaCl (1 M)	58.45	0.055123	5.512333953
Water	1000	0.943085	94.30853641
Total	1060.349		

Appendix C – Glossary

Antigen- Any foreign material that is specifically bound by a specific antibody.

Antigen-binding site- Part of an immunoglobulin molecule that binds an antigen specifically.

Batch mode- the most commonly used type of fermentation, in which microbes are added to a sterile nutrient broth and allowed to ferment without the addition of further nutrients (except oxygen).

Chromatography- a technique used to separate molecules based on their different physical or chemical properties.

Crossflow- Flow of solution adjacent or parallel to the surface of the membrane. This contrasts with direct flow seen in traditional filters, in which the liquid flows perpendicular to the surface of the filter. In crossflow, only a fraction of the crossflow solution passes through the membrane.

Diafiltration- A crossflow filtration process allowing for the transfer of low molecular weight species, water and/or solvents through a membrane without changing the solution volume. This process is used for purifying retained large molecular weight species, increasing the recovery of low molecular weight species, buffer exchange and simply changing the properties of a given solution.

Dalton (Da)- A unit of mass that equals the weight of a hydrogen atom, or 1.657×10^{-24} g.

Fab fragment- “fragment antigen binding”; Fragment of antibody containing the antigen binding site, generated by the cleavage of the antibody with the enzyme papain, which cuts at the hinge region N-terminally to the inter-H-chain disulphide bond and generates two Fab fragments from one antibody molecule.

Fc fragment- “fragment crystallizable”; Fragment of the antibody without antigen-binding sites, generated by cleavage with papain; the Fc fragment contains the C-terminal domains of the heavy immunoglobulin chains.

Fed-batch mode- fermentation in which substrate is added incrementally throughout the process.

Flux: The amount of solution that passes through a unit of membrane area in a given amount of time. For example, a filter might have a flux of 1 liter per minute per square centimeter.

Fouling- Contamination (plugging) of the membrane, either decreasing flux, or increasing differential pressure or TMP. Membrane fouling may necessitate a flux maintenance procedure or a membrane cleaning.

Hinge Region- a flexible, open segment of an antibody that allows bending of the molecule. The hinge region is located between the Fab and Fc fragments and is susceptible to enzymatic cleavage.

Hydrodynamic Diameter- the diameter of a hard sphere that diffuses at the same rate as the molecule, taking hydration and shape effects into account.

Inoculation- a standard procedure to initialize the operation of a bioreactor by adding a small amount of cells. The initial amount of cells are cultured in a carefully controlled medium and are allowed to undergo division and growth to a desired cell density within the bioreactor.

Ion Exchange Chromatography- utilizes charge properties to bind either negatively or positively charged ions. There are two types:

Cation Exchange- column with negative charge, binds positively charged particles - used at a low enough pH that the desired antibody binds to the column while anions flow through.

Anion Exchange- column with positive charge, binds negatively charged particles – binds DNA, endotoxin, retrovirus.

Lactate (lactic acid)- a byproduct of carbohydrate metabolism (anaerobic metabolism) that plays a role in several biochemical processes; produced (for example) as a result of anaerobic respiration in muscles and red blood cells when glycogen rather than oxygen is used as an energy source for respiration.

Membrane Filtration- Membrane filtration is a pressure driven process that uses a semi-permeable (porous) membrane to separate particulate matter from soluble components in the carrier fluid such as water.

Monoclonal- Literally, coming from a single clone. A clone is the progeny of a single cell. In immunology, monoclonal generally describes a preparation of antibody that is monogenous, or cells of a single specificity.

Monoclonal Antibodies- antibodies that come from plasma cells that produce a single antibody of known specificity.

Papain- a nonspecific, thiol-endopeptidase that has a sulfhydryl group in the active site, which must be in the reduced form for activity. When antibody molecules are incubated with papain in the presence of cysteine, one or more peptide bonds in the hinge region are split, producing three fragments of similar size: two Fab fragments and one Fc fragment. The Fc fragments can be separated from the Fab fragments using immobilized Protein A or by ion exchange chromatography.

Protein A- A 42-kDa monomeric protein from *Staphylococcus aureus* bacteria, protein A lacks cysteine residues and binds to the Fc portion of immunoglobulins. It is used extensively in affinity chromatography; ELISAs; and immunoblotting, -precipitation, and -histochemistry.

PEGylation- the process of covalent attachment of poly(ethylene glycol) polymer chains to another molecule, normally a drug or therapeutic protein. PEGylation is routinely achieved by incubation of a reactive derivative of PEG with the target macromolecule. The covalent attachment of PEG to a drug or therapeutic protein can "mask" the agent from the host's immune system (reduced immunogenicity and antigenicity), increase the hydrodynamic size (size in solution) of the agent which prolongs its circulatory time by reducing renal clearance. PEGylation can also provide water solubility to hydrophobic drugs and proteins.

Serum- fluid portion of blood; retains antibodies present in whole blood.

Titer- the quantity of one substance required to produce a reaction with a specific volume of another; also the number/measure of antibodies detected in blood or media.

TNF-alpha – “Tumor necrosis factor-alpha” is a cytokine involved in systemic inflammation and is a member of a group of cytokines that stimulate the acute phase reaction. The primary role of TNF is in the regulation of immune cells. TNF is also able to induce apoptotic cell death, to induce inflammation, and to inhibit tumorigenesis and viral replication.

Ultrafiltration (UF)- high-level filtration system for the treatment of water and other liquids. Liquids are forced through a membrane with extremely fine pores to filter colloids and molecules between 0.002 and 0.1 microns in size. Ultrafiltration is capable of removing solids, bacteria and viruses .

Validation- Establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality attributes.

Validation protocol- A written plan stating how validation will be conducted, including test parameters, product characteristics, production equipment, and decision points on what constitutes acceptable test results.

Viral filtration- retrovirus and parvovirus filters remove small viruses of 50 nm and 20 nm sizes and larger, leaving target protein in stream.

Water for Injection (WFI)- highly purified water used for medical purposes.

Appendix D – SuperPro Designer Stream Reports

1. BIOREACTION OVERALL PROCESS DATA

Annual Operating Time	7836.52	h
Annual Throughput	1887.70	kg MP
Batch Throughput	34.32	kg MP
Recipe Batch Time	807.66	h
Recipe Cycle Time	130.16	h
Number of Batches per Year	55.00	
MP = Main Product = Flow of MAB in stream To Primary Recovery		

STREAM DETAILS

Stream Name	Innoculum Media-1	S-101	Innoculum Media-2	S-102
Source	INPUT	P-1	INPUT	P-2
Destination	P-1	P-2	P-2	P-3
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	37.00	25.00	37.00
Pressure (bar)	1.01	1.88	1.01	1.80
Density (g/L)	1007.62	997.17	1007.62	997.14
Component Flowrates (kg/batch)				
Amino Acids	0.00	0.00	0.01	0.01
Biomass*	0.00	0.00	0.00	0.00
Dead Biomass	0.00	0.00	0.00	0.00
Glucose	0.01	0.01	0.05	0.06
Glutamine	0.00	0.00	0.01	0.01
Inorganic Salts	0.03	0.03	0.11	0.14
Lactate	0.00	0.00	0.00	0.00
MAB	0.00	0.00	0.00	0.00
Other Media Components	0.00	0.00	0.00	0.00
Vitamins	0.00	0.00	0.00	0.00
Water	0.00	0.00	0.00	0.00
WFI	2.11	2.11	8.69	10.80
TOTAL (kg/batch)	2.15	2.15	8.87	11.02
TOTAL (L/batch)	2.14	2.16	8.80	11.05
Stream Name	Innoculum Media-3	Vent-1	S-103	Innoculum Media-4
Source	INPUT	P-3	P-3	INPUT
Destination	P-3	OUTPUT	P-4	P-4
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00

Temperature (°C)	25.00	37.00	37.00	25.00
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	1007.62	1.17	997.12	1007.62
Component Flowrates (kg/batch)				
Amino Acids	0.08	0.00	0.09	0.31
Biomass	0.00	0.00	0.01	0.00
Carb. Dioxide	0.00	0.01	0.00	0.00
Dead Biomass	0.00	0.00	0.00	0.00
Glucose	0.32	0.00	0.37	1.32
Glutamine	0.04	0.00	0.04	0.15
Inorganic Salts	0.77	0.00	0.88	3.21
Lactate	0.00	0.00	0.01	0.00
MAB	0.00	0.00	0.00	0.00
Nitrogen	0.00	0.06	0.00	0.00
Other Media Components	0.01	0.00	0.01	0.03
Oxygen	0.00	0.00	0.00	0.00
Vitamins	0.00	0.00	0.00	0.01
Water	0.00	0.00	0.03	0.00
WFI	59.25	0.00	70.05	246.87
TOTAL (kg/batch)	60.46	0.08	71.49	251.90
TOTAL (L/batch)	60.00	64.29	71.70	250.00

Stream Name	Vent-2	S-104	S-108	Air Stream-1
Source	P-4	P-4	P-8	INPUT
Destination	OUTPUT	P-9	P-9	P-9
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	37.00	37.00	25.02	25.00
Pressure (bar)	1.01	1.01	5.38	1.01
Density (g/L)	1.17	997.09	1006.20	1.18
Component Flowrates (kg/batch)				
Amino Acids	0.00	0.39	1.36	0.00
Biomass	0.00	0.07	0.00	0.00
Carb. Dioxide	0.05	0.00	0.00	0.00
Dead Biomass	0.00	0.01	0.00	0.00
Glucose	0.00	1.64	5.77	0.00
Glutamine	0.00	0.19	0.67	0.00
Inorganic Salts	0.00	3.98	13.97	0.00
Lactate	0.00	0.05	0.00	0.00
MAB	0.00	0.02	0.00	0.00
Nitrogen	0.27	0.00	0.00	2780.96
Other Media Components	0.00	0.03	0.12	0.00
Oxygen	0.01	0.00	0.00	844.25
Vitamins	0.00	0.02	0.06	0.00
Water	0.00	0.13	0.00	0.00

WFI	0.00	316.91	648.69	0.00
TOTAL (kg/batch)	0.33	323.45	670.64	3625.21
TOTAL (L/batch)	284.41	324.39	666.51	3074994.50

Stream Name	Vent-3	S-109	WFI-1	SF Media-1
Source	P-9	P-9	INPUT	INPUT
Destination	OUTPUT	P-10	P-5	P-5
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	37.00	37.00	25.00	25.00
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	1.13	993.33	994.70	1640.37
Component Flowrates (kg/batch)				
Amino Acids	0.00	0.35	0.00	1.36
Biomass	0.00	7.80	0.00	0.00
Carb. Dioxide	15.66	0.00	0.00	0.00
Dead Biomass	0.00	0.80	0.00	0.00
Glucose	0.00	1.48	0.00	5.77
Glutamine	0.00	0.17	0.00	0.67
Inorganic Salts	0.00	3.59	0.00	13.97
Lactate	0.00	5.53	0.00	0.00
MAB	0.00	1.60	0.00	0.00
Nitrogen	2781.89	0.00	0.00	0.00
Other Media Components	0.00	0.03	0.00	0.12
Oxygen	821.97	0.00	0.00	0.00
Vitamins	0.00	0.02	0.00	0.06
Water	0.00	14.01	0.00	0.00
WFI	0.00	965.61	648.69	0.00
TOTAL (kg/batch)	3619.51	1000.99	648.69	21.95
TOTAL (L/batch)	3190145.66	1007.72	652.15	13.38

Stream Name	S-105	S-106	S-107	S-110
Source	P-5	P-6	P-7	P-10
Destination	P-6	P-7	P-8	P-15
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.01	25.01	37.02
Pressure (bar)	3.38	4.38	4.38	2.74
Density (g/L)	1006.21	1006.21	1006.21	993.32
Component Flowrates (kg/batch)				
Amino Acids	1.36	1.36	1.36	0.35
Biomass	0.00	0.00	0.00	7.80
Dead Biomass	0.00	0.00	0.00	0.80
Glucose	5.77	5.77	5.77	1.48
Glutamine	0.67	0.67	0.67	0.17

Inorganic Salts	13.97	13.97	13.97	3.59
Lactate	0.00	0.00	0.00	5.53
MAB	0.00	0.00	0.00	1.60
Other Media Components	0.12	0.12	0.12	0.03
Vitamins	0.06	0.06	0.06	0.02
Water	0.00	0.00	0.00	14.01
WFI	648.69	648.69	648.69	965.61
TOTAL (kg/batch)	670.64	670.64	670.64	1000.99
TOTAL (L/batch)	666.50	666.51	666.51	1007.72

Stream Name	S-114	Air Stream-2	Vent-4	S-115
Source	P-14	INPUT	P-15	P-15
Destination	P-15	P-15	OUTPUT	P-16
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.02	25.00	37.00	37.00
Pressure (bar)	5.38	1.01	1.01	1.01
Density (g/L)	1006.07	1.18	1.13	993.16
Component Flowrates (kg/batch)				
Amino Acids	4.18	0.00	0.00	0.91
Biomass	0.00	0.00	0.00	27.78
Carb. Dioxide	0.00	0.00	40.47	0.00
Dead Biomass	0.00	0.00	0.00	2.85
Glucose	17.68	0.00	0.00	3.83
Glutamine	2.05	0.00	0.00	0.44
Inorganic Salts	42.82	0.00	0.00	9.28
Lactate	0.00	0.00	0.00	19.70
MAB	0.00	0.00	0.00	5.70
Nitrogen	0.00	8626.38	8629.25	0.00
Other Media Components	0.37	0.00	0.00	0.08
Oxygen	0.00	2618.80	2561.36	0.00
Vitamins	0.18	0.00	0.00	0.04
Water	0.00	0.00	0.00	49.87
WFI	2011.29	0.00	0.00	2976.90
TOTAL (kg/batch)	2078.55	11245.18	11231.08	3097.38
TOTAL (L/batch)	2066.00	9536104.80	9900239.90	3118.71

Stream Name	S-111	S-112	S-113	WFI-2
Source	P-11	P-12	P-13	INPUT
Destination	P-12	P-13	P-14	P-11
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.01	25.01	25.00
Pressure (bar)	3.38	4.38	4.38	1.01
Density (g/L)	1006.08	1006.08	1006.08	994.70

Component Flowrates (kg/batch)				
Amino Acids	4.18	4.18	4.18	0.00
Glucose	17.68	17.68	17.68	0.00
Glutamine	2.05	2.05	2.05	0.00
Inorganic Salts	42.82	42.82	42.82	0.00
Other Media Components	0.37	0.37	0.37	0.00
Vitamins	0.18	0.18	0.18	0.00
WFI	2011.29	2011.29	2011.29	2011.29
TOTAL (kg/batch)	2078.55	2078.55	2078.55	2011.29
TOTAL (L/batch)	2065.99	2066.00	2066.00	2022.00

Stream Name	SF Media-2	S-116	S-120	S-124
Source	INPUT	P-16	P-20	P-24
Destination	P-11	P-25	P-25	P-25
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	37.01	25.02	25.02
Pressure (bar)	1.01	2.01	5.38	5.38
Density (g/L)	1640.37	993.16	1005.97	1083.65
Component Flowrates (kg/batch)				
Amino Acids	4.18	0.91	10.74	17.12
Biomass	0.00	27.78	0.00	0.00
Dead Biomass	0.00	2.85	0.00	0.00
Glucose	17.68	3.83	45.45	72.46
Glutamine	2.05	0.44	5.26	8.38
Inorganic Salts	42.82	9.28	110.10	175.52
Lactate	0.00	19.70	0.00	0.00
MAB	0.00	5.70	0.00	0.00
Other Media Components	0.37	0.08	0.95	1.52
Vitamins	0.18	0.04	0.45	0.72
Water	0.00	49.87	0.00	0.00
WFI	0.00	2976.90	5222.20	897.89
TOTAL (kg/batch)	67.26	3097.38	5395.15	1173.60
TOTAL (L/batch)	41.00	3118.72	5363.16	1083.00

Stream Name	Air Stream-3	Vent-5	To Primary Recovery	WFI-3
Source	INPUT	P-25	P-25	INPUT
Destination	P-25	OUTPUT	OUTPUT	P-17
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	37.00	37.00	25.00
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	1.18	1.14	994.61	994.70
Component Flowrates (kg/batch)				

Amino Acids	0.00	0.00	3.49	0.00
Biomass	0.00	0.00	167.26	0.00
Carb. Dioxide	0.00	282.39	0.00	0.00
Dead Biomass	0.00	0.00	17.14	0.00
Glucose	0.00	0.00	14.75	0.00
Glutamine	0.00	0.00	1.71	0.00
Inorganic Salts	0.00	0.00	35.72	0.00
Lactate	0.00	0.00	118.59	0.00
MAB	0.00	0.00	34.32	0.00
Nitrogen	5355.96	5364.91	0.00	0.00
Other Media Components	0.00	0.00	0.31	0.00
Oxygen	1625.97	1221.84	0.00	0.00
Vitamins	0.00	0.00	0.15	0.00
Water	0.00	0.00	300.26	0.00
WFI	0.00	0.00	9096.99	5222.20
TOTAL (kg/batch)	6981.92	6869.14	9790.67	5222.20
TOTAL (L/batch)	5920790.79	6009112.24	9843.78	5250.00

Stream Name	SF Media-3	S-117	S-118	S-119
Source	INPUT	P-17	P-18	P-19
Destination	P-17	P-18	P-19	P-20
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.01	25.01
Pressure (bar)	1.01	3.38	4.38	4.38
Density (g/L)	1640.37	1005.97	1005.97	1005.97
Component Flowrates (kg/batch)				
Amino Acids	10.74	10.74	10.74	10.74
Glucose	45.45	45.45	45.45	45.45
Glutamine	5.26	5.26	5.26	5.26
Inorganic Salts	110.10	110.10	110.10	110.10
Other Media Components	0.95	0.95	0.95	0.95
Vitamins	0.45	0.45	0.45	0.45
WFI	0.00	5222.20	5222.20	5222.20
TOTAL (kg/batch)	172.96	5395.15	5395.15	5395.15
TOTAL (L/batch)	105.44	5363.12	5363.14	5363.14

Stream Name	WFI-4	SF Media-4	S-121	S-122
Source	INPUT	INPUT	P-21	P-22
Destination	P-21	P-21	P-22	P-23
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.01
Pressure (bar)	1.01	1.01	3.38	4.38
Density (g/L)	994.70	1640.37	1083.66	1083.66

Component Flowrates (kg/batch)				
Amino Acids	0.00	17.32	17.12	17.12
Glucose	0.00	73.29	72.46	72.46
Glutamine	0.00	8.48	8.38	8.38
Inorganic Salts	0.00	177.52	175.52	175.52
Other Media Components	0.00	1.53	1.52	1.52
Vitamins	0.00	0.73	0.72	0.72
WFI	908.17	0.00	897.89	897.89
TOTAL (kg/batch)	908.17	278.86	1173.60	1173.60
TOTAL (L/batch)	913.00	170.00	1082.99	1083.00

Stream Name	S-123
Source	P-23
Destination	P-24
Stream Properties	
Activity (U/ml)	0.00
Temperature (°C)	25.01
Pressure (bar)	4.38
Density (g/L)	1083.66
Component Flowrates (kg/batch)	
Amino Acids	17.12
Glucose	72.46
Glutamine	8.38
Inorganic Salts	175.52
Other Media Components	1.52
Vitamins	0.72
WFI	897.89
TOTAL (kg/batch)	1173.60
TOTAL (L/batch)	1083.00

2. PAPAIN CLEAVAGE OVERALL PROCESS DATA

Annual Operating Time	7912.36	h
Annual Throughput	8410.56	kg MP
Batch Throughput	17.60	kg MP
Recipe Batch Time	38.96	h
Recipe Cycle Time	16.51	h
Number of Batches per Year	478.00	
MP = Main Product = Flow of MAb Fab Fragments in stream To IEX		

STREAM DETAILS

Stream Name	From Bioreactor	S-201	S-202	S-203
Source	INPUT	P-26	P-27	P-28
Destination	P-26	P-27	P-28	P-29
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.02	25.00
Pressure (bar)	1.01	1.01	2.74	2.74
Density (g/L)	999.04	999.04	999.03	999.11
Component Flowrates (kg/batch)				
Amino Acids	3.49	3.49	3.49	3.15
Biomass	167.26	167.26	167.26	3.35
Dead Biomass	17.14	17.14	17.14	15.49
Glucose	14.75	14.75	14.75	13.33
Glutamine	1.71	1.71	1.71	1.54
Inorganic Salts	35.72	35.72	35.72	32.28
Lactate	118.59	118.59	118.59	107.16
MAB	34.32	34.32	34.32	31.02
Other Media Components	0.31	0.31	0.31	0.28
Vitamins	0.15	0.15	0.15	0.13
Water	300.26	300.26	300.26	271.33
WFI	9096.99	9096.99	9096.99	8220.53
TOTAL (kg/batch)	9790.67	9790.67	9790.67	8699.58
TOTAL (L/batch)	9800.09	9800.09	9800.15	8707.30
Stream Name	Waste-5	S-206	Vent-7	S-207
Source	P-28	P-31	P-32	P-32
Destination	OUTPUT	P-32	OUTPUT	P-33
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.04	25.04	25.04
Pressure (bar)	2.74	6.18	1.01	1.01
Density (g/L)	998.45	999.10	1.18	999.10

Component Flowrates (kg/batch)

Amino Acids	0.34	3.15	0.00	3.15
Biomass	163.92	0.00	0.00	0.00
Dead Biomass	1.65	15.48	0.00	15.48
Glucose	1.42	13.32	0.00	13.32
Glutamine	0.16	1.54	0.00	1.54
Inorganic Salts	3.44	32.27	0.00	32.27
Lactate	11.43	107.12	0.00	107.12
MAB	3.31	31.00	0.00	31.00
Nitrogen	0.00	0.00	7.87	0.00
Other Media Components	0.03	0.28	0.00	0.28
Oxygen	0.00	0.00	2.39	0.00
Vitamins	0.01	0.13	0.00	0.13
Water	28.93	271.22	0.00	271.22
WFI	876.46	8217.36	0.00	8217.36
TOTAL (kg/batch)	1091.09	8692.87	10.26	8692.87
TOTAL (L/batch)	1092.79	8700.69	8701.85	8700.69

Stream Name	S-204	S-205	Waste-6	S-208
Source	P-29	P-30	P-30	P-33
Destination	P-30	P-31	OUTPUT	P-34
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.02	25.02	25.02	25.05
Pressure (bar)	4.46	4.46	4.46	2.74
Density (g/L)	999.11	999.11	996.90	999.10

Component Flowrates (kg/batch)

Amino Acids	3.15	3.15	0.00	3.15
Biomass	3.35	0.00	3.35	0.00
Dead Biomass	15.49	15.48	0.01	15.48
Glucose	13.33	13.32	0.01	13.32
Glutamine	1.54	1.54	0.00	1.54
Inorganic Salts	32.28	32.27	0.01	32.27
Lactate	107.16	107.12	0.04	107.12
MAB	31.02	31.00	0.01	31.00
Other Media Components	0.28	0.28	0.00	0.28
Vitamins	0.13	0.13	0.00	0.13
Water	271.33	271.22	0.11	271.22
WFI	8220.53	8217.36	3.18	8217.36
TOTAL (kg/batch)	8699.58	8692.87	6.71	8692.87
TOTAL (L/batch)	8707.36	8700.63	6.73	8700.75

Stream Name	Waste-7	S-209	S-210	Digest Buffer
Source	P-34	P-34	P-35	INPUT

Destination	OUTPUT	P-35	P-36	P-36
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.77	25.77	25.84	25.00
Pressure (bar)	2.74	2.74	9.63	1.01
Density (g/L)	998.85	998.76	998.73	1004.70
Component Flowrates (kg/batch)				
Amino Acids	2.60	0.55	0.55	0.00
Cysteine-HCl	0.00	0.00	0.00	5.45
Dead Biomass	12.77	2.71	2.71	0.00
EDTA Disodium	0.00	0.00	0.00	9.02
Glucose	10.99	2.33	2.33	0.00
Glutamine	1.27	0.27	0.27	0.00
Inorganic Salts	26.62	5.65	5.65	0.00
Lactate	88.38	18.74	18.74	0.00
MAB	0.00	31.00	31.00	0.00
Other Media Components	0.23	0.05	0.05	0.00
Sodium Phosphate	0.00	0.00	0.00	4.20
Vitamins	0.11	0.02	0.02	0.00
Water	223.76	47.46	47.46	0.00
WFI	6779.48	1437.88	1437.88	1537.23
TOTAL (kg/batch)	7146.21	1546.66	1546.66	1555.90
TOTAL (L/batch)	7154.47	1548.59	1548.63	1548.63

Stream Name	Papain	Waste-8	S-211	S-212
Source	INPUT	P-36	P-36	P-37
Destination	P-36	OUTPUT	P-37	P-38
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	37.00	37.00	37.26
Pressure (bar)	1.01	10.54	2.13	27.13
Density (g/L)	994.70	990.33	994.27	994.17
Component Flowrates (kg/batch)				
Amino Acids	0.00	0.00	0.55	0.55
Cysteine-HCl	0.00	0.00	5.45	5.45
Dead Biomass	0.00	0.00	2.71	2.71
EDTA Disodium	0.00	0.00	9.02	9.02
Glucose	0.00	0.00	2.33	2.33
Glutamine	0.00	0.00	0.27	0.27
Inorganic Salts	0.00	0.00	5.65	5.65
Lactate	0.00	0.00	18.74	18.74
MAB	0.00	0.00	1.55	1.55
MAb Fab Fragments	0.00	0.00	19.64	19.64
MAb Fc Fragments	0.00	0.00	9.82	9.82
Other Media Components	0.00	0.00	0.05	0.05

Papain	1540.43	0.00	1540.43	1540.43
Sodium Phosphate	0.00	0.00	4.20	4.20
Vitamins	0.00	0.00	0.02	0.02
Water	0.00	0.00	47.46	47.46
WFI	1540.43	2709.32	1806.21	1806.21
TOTAL (kg/batch)	3080.85	2709.32	3474.09	3474.09
TOTAL (L/batch)	3097.25	2735.77	3494.11	3494.45

Stream Name	Tris-HCl	Waste-9	S-213	ProtA-Equill.
Source	INPUT	P-38	P-38	INPUT
Destination	P-38	OUTPUT	P-39	P-40
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	4.00	28.92	25.44	25.00
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	1096.65	1004.81	1021.57	998.35
Component Flowrates (kg/batch)				
Amino Acids	0.00	0.04	0.51	0.00
Cysteine-HCl	0.00	0.41	5.03	0.00
Dead Biomass	0.00	0.21	2.50	0.00
EDTA Disodium	0.00	0.68	8.34	0.00
EDTA, Sodium	0.00	0.00	0.00	5.25
Glucose	0.00	0.18	2.15	0.00
Glutamine	0.00	0.02	0.25	0.00
Inorganic Salts	0.00	0.43	5.22	0.00
Lactate	0.00	1.42	17.33	0.00
MAB	0.00	0.12	1.43	0.00
MAb Fab Fragments	0.00	1.49	18.15	0.00
MAb Fc Fragments	0.00	0.74	9.07	0.00
Other Media Components	0.00	0.00	0.05	0.00
Papain	0.00	1540.43	0.00	0.00
Sodium Chloride	0.00	0.00	0.00	2.62
Sodium Phosphate	0.00	0.32	3.88	0.00
TRIS Base	0.00	0.00	0.00	2.62
TRIS HCl	206.78	45.86	160.92	7.87
Vitamins	0.00	0.00	0.02	0.00
Water	0.00	3.59	43.87	0.00
WFI	2340.66	655.84	3491.04	2604.09
TOTAL (kg/batch)	2547.44	2251.77	3769.77	2622.45
TOTAL (L/batch)	2322.93	2240.98	3690.18	2626.78

Stream Name	ProtA-Wash	ProtA-Elut.	ProtA-Reg.	S-214
Source	INPUT	INPUT	INPUT	P-39
Destination	P-40	P-40	P-40	P-40

Stream Properties

Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	4.00	4.00	4.00	25.52
Pressure (bar)	1.01	1.01	1.01	7.91
Density (g/L)	1006.01	1002.70	1003.19	1021.54
Component Flowrates (kg/batch)				
Amino Acids	0.00	0.00	0.00	0.51
Acetic-Acid	0.00	15.80	0.00	0.00
Cysteine-HCl	0.00	0.00	0.00	5.03
Dead Biomass	0.00	0.00	0.00	2.50
EDTA Disodium	0.00	0.00	0.00	8.34
EDTA, Sodium	6.34	0.00	0.00	0.00
Glucose	0.00	0.00	0.00	2.15
Glutamine	0.00	0.00	0.00	0.25
Inorganic Salts	0.00	0.00	0.00	5.22
Lactate	0.00	0.00	0.00	17.33
MAB	0.00	0.00	0.00	1.43
MAb Fab Fragments	0.00	0.00	0.00	18.15
MAb Fc Fragments	0.00	0.00	0.00	9.07
Other Media Components	0.00	0.00	0.00	0.05
Sodium Chloride	3.17	0.00	0.00	0.00
Sodium Citrate	0.00	0.00	2.85	0.00
Sodium Phosphate	0.00	0.00	0.00	3.88
TRIS Base	3.17	0.00	0.00	0.00
TRIS HCl	9.51	0.00	0.00	160.92
Vitamins	0.00	0.00	0.00	0.02
Water	0.00	0.00	0.00	43.87
WFI	3148.88	2618.08	1578.25	3491.04
TOTAL (kg/batch)	3171.08	2633.88	1581.09	3769.77
TOTAL (L/batch)	3152.13	2626.78	1576.07	3690.28

Stream Name	S-215	Waste-11	WFI-5	S-219
Source	P-40	P-40	INPUT	P-44
Destination	P-41	OUTPUT	P-45	P-45
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	20.81	10.17	4.00	20.88
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	1017.35	1002.67	1002.36	1017.31
Component Flowrates (kg/batch)				
Amino Acids	0.51	0.00	0.00	0.51
Acetic-Acid	6.32	9.48	0.00	6.32
Cysteine-HCl	5.03	0.00	0.00	5.03
Dead Biomass	2.50	0.00	0.00	0.00
EDTA Disodium	8.34	0.00	0.00	8.34

EDTA, Sodium	0.00	11.59	0.00	0.00
Glucose	2.15	0.00	0.00	2.15
Glutamine	0.25	0.00	0.00	0.25
Inorganic Salts	5.22	0.00	0.00	5.22
Lactate	17.33	0.00	0.00	17.32
MAB	0.00	1.43	0.00	0.00
MAb Fab Fragments	18.15	0.00	0.00	18.14
MAb Fc Fragments	0.00	9.07	0.00	0.00
Other Media Components	0.05	0.00	0.00	0.05
Sodium Chloride	0.00	5.79	0.00	0.00
Sodium Citrate	0.00	2.85	0.00	0.00
Sodium Phosphate	3.88	0.00	0.00	3.88
TRIS Base	0.00	5.79	0.00	0.00
TRIS HCl	160.92	17.38	0.00	160.84
Vitamins	0.02	0.00	0.00	0.02
Water	43.87	0.00	0.00	43.84
WFI	4538.27	8902.06	1894.89	4535.98
TOTAL (kg/batch)	4812.81	8965.45	1894.89	4807.88
TOTAL (L/batch)	4730.72	8941.57	1890.43	4726.08

Stream Name	WFI-6	S-220	WFI-out	Waste-13
Source	INPUT	P-45	P-45	P-45
Destination	P-45	P-44	OUTPUT	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	4.00	16.41	4.00	16.41
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	1002.36	1000.64	1002.36	1014.95
Component Flowrates (kg/batch)				
Amino Acids	0.00	0.01	0.00	0.50
Acetic-Acid	0.00	0.17	0.00	6.15
Cysteine-HCl	0.00	0.13	0.00	4.90
EDTA Disodium	0.00	0.22	0.00	8.12
Glucose	0.00	0.06	0.00	2.10
Glutamine	0.00	0.01	0.00	0.24
Impurities	0.00	0.26	0.00	0.28
Inorganic Salts	0.00	0.14	0.00	5.08
Lactate	0.00	0.46	0.00	16.86
MAb Fab Fragments	0.00	17.60	0.00	0.00
Other Media Components	0.00	0.00	0.00	0.04
Sodium Phosphate	0.00	0.10	0.00	3.78
TRIS HCl	0.00	4.29	0.00	156.55
Vitamins	0.00	0.00	0.00	0.02
Water	0.00	1.17	0.00	42.68
WFI	501.18	924.60	501.18	5506.27

TOTAL (kg/batch)	501.18	949.22	501.18	5753.55
TOTAL (L/batch)	500.00	948.62	500.00	5668.83

Stream Name	S-218	Vent-10	S-221	S-216
Source	P-43	P-44	P-44	P-41
Destination	P-44	OUTPUT	P-46	P-42
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	20.88	19.57	16.42	20.84
Pressure (bar)	7.91	1.01	1.01	4.46
Density (g/L)	1017.31	1.20	1000.63	1017.34
Component Flowrates (kg/batch)				
Amino Acids	0.51	0.00	0.01	0.51
Acetic-Acid	6.32	0.00	0.17	6.32
Cysteine-HCl	5.03	0.00	0.13	5.03
Dead Biomass	0.00	0.00	0.00	2.50
EDTA Disodium	8.34	0.00	0.22	8.34
Glucose	2.15	0.00	0.06	2.15
Glutamine	0.25	0.00	0.01	0.25
Impurities	0.00	0.00	0.26	0.00
Inorganic Salts	5.22	0.00	0.14	5.22
Lactate	17.32	0.00	0.46	17.33
MAb Fab Fragments	18.14	0.00	17.60	18.15
Nitrogen	0.00	5.08	0.00	0.00
Other Media Components	0.05	0.00	0.00	0.05
Oxygen	0.00	1.54	0.00	0.00
Sodium Phosphate	3.88	0.00	0.10	3.88
TRIS HCl	160.84	0.00	4.29	160.92
Vitamins	0.02	0.00	0.00	0.02
Water	43.84	0.00	1.17	43.87
WFI	4535.98	0.00	924.60	4538.27
TOTAL (kg/batch)	4807.88	6.62	949.22	4812.81
TOTAL (L/batch)	4726.08	5511.15	948.62	4730.78

Stream Name	S-217	Waste-12	Polysorb80	S-222
Source	P-42	P-42	INPUT	P-46
Destination	P-43	OUTPUT	P-47	P-47
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	20.84	20.84	4.00	16.45
Pressure (bar)	4.46	4.46	1.01	4.46
Density (g/L)	1017.32	1033.66	881.61	1000.62
Component Flowrates (kg/batch)				
Amino Acids	0.51	0.00	0.00	0.01
Acetic-Acid	6.32	0.00	0.00	0.17

Cysteine-HCl	5.03	0.00	0.00	0.13
Dead Biomass	0.00	2.50	0.00	0.00
EDTA Disodium	8.34	0.00	0.00	0.22
Glucose	2.15	0.00	0.00	0.06
Glutamine	0.25	0.00	0.00	0.01
Impurities	0.00	0.00	0.00	0.26
Inorganic Salts	5.22	0.00	0.00	0.14
Lactate	17.32	0.01	0.00	0.46
MAb Fab Fragments	18.14	0.01	0.00	17.60
Other Media Components	0.05	0.00	0.00	0.00
Polysorbate 80	0.00	0.00	0.10	0.00
Sodium Phosphate	3.88	0.00	0.00	0.10
TRIS HCl	160.84	0.08	0.00	4.29
Vitamins	0.02	0.00	0.00	0.00
Water	43.84	0.02	0.00	1.17
WFI	4535.98	2.29	0.10	924.60
TOTAL (kg/batch)	4807.88	4.93	0.19	949.22
TOTAL (L/batch)	4726.01	4.77	0.22	948.63

Stream Name	Vent-11	S-223	S-224	To IEX
Source	P-47	P-47	P-48	P-49
Destination	OUTPUT	P-48	P-49	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	16.46	16.45	16.49	16.49
Pressure (bar)	1.01	1.01	4.46	4.46
Density (g/L)	1.21	1000.59	1000.58	1000.58
Component Flowrates (kg/batch)				
Amino Acids	0.00	0.01	0.01	0.01
Acetic-Acid	0.00	0.17	0.17	0.17
Cysteine-HCl	0.00	0.13	0.13	0.13
EDTA Disodium	0.00	0.22	0.22	0.22
Glucose	0.00	0.06	0.06	0.06
Glutamine	0.00	0.01	0.01	0.01
Impurities	0.00	0.26	0.26	0.26
Inorganic Salts	0.00	0.14	0.14	0.14
Lactate	0.00	0.46	0.46	0.46
MAb Fab Fragments	0.00	17.60	17.60	17.60
Nitrogen	0.86	0.00	0.00	0.00
Other Media Components	0.00	0.00	0.00	0.00
Oxygen	0.26	0.00	0.00	0.00
Polysorbate 80	0.00	0.10	0.10	0.10
Sodium Phosphate	0.00	0.10	0.10	0.10
TRIS HCl	0.00	4.29	4.29	4.29
Vitamins	0.00	0.00	0.00	0.00

Water	0.00	1.17	1.17	1.17
WFI	0.00	924.69	924.69	924.69
TOTAL (kg/batch)	1.12	949.41	949.41	949.41
TOTAL (L/batch)	918.63	948.85	948.86	948.86

2A. NO CLEAVAGE OVERALL PROCESS DATA

Annual Operating Time	7918.74	h
Annual Throughput	0.00	kg MP
Batch Throughput	0.00	kg MP
Recipe Batch Time	20.87	h
Recipe Cycle Time	15.92	h
Number of Batches per Year	497.00	
MP = Main Product = Flow of MAb Fab Fragments in stream To IEX		

STREAM DETAILS

Stream Name	From Bioreactor	S-201	ProtA- Equil.	ProtA- Wash
Source	INPUT	P-26	INPUT	INPUT
Destination	P-26	P-27	P-36	P-36
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	4.00
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	996.55	996.55	998.35	1006.01
Component Flowrates (kg/batch)				
Amino Acids	0.29	0.29	0.00	0.00
Biomass	184.88	184.88	0.00	0.00
Dead Biomass	18.94	18.94	0.00	0.00
EDTA, Sodium	0.00	0.00	22.27	26.93
Glucose	1.23	1.23	0.00	0.00
Glutamine	0.14	0.14	0.00	0.00
Inorganic Salts	2.98	2.98	0.00	0.00
Lactate	131.08	131.08	0.00	0.00
MAB	37.94	37.94	0.00	0.00
Other Media Components	0.03	0.03	0.00	0.00
Sodium Chloride	0.00	0.00	11.14	13.47
TRIS Base	0.00	0.00	11.14	13.47
TRIS HCl	0.00	0.00	33.41	40.40
Vitamins	0.01	0.01	0.00	0.00
Water	331.88	331.88	0.00	0.00
WFI	13825.29	13825.29	11058.22	13371.67
TOTAL (kg/batch)	14534.70	14534.70	11136.17	13465.93
TOTAL (L/batch)	14585.02	14585.02	11154.57	13385.48
Stream Name	ProtA- Elut.	ProtA- Reg.	S-215	S-216
Source	INPUT	INPUT	P-35	P-36
Destination	P-36	P-36	P-36	P-37

Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	4.00	4.00	4.07	4.00
Pressure (bar)	1.01	1.01	9.63	1.01
Density (g/L)	1002.70	1003.19	1004.22	1002.70
Component Flowrates (kg/batch)				
Amino Acids	0.00	0.00	0.03	0.00
Acetic-Acid	67.11	0.00	0.00	26.84
Dead Biomass	0.00	0.00	1.72	0.00
Glucose	0.00	0.00	0.11	0.00
Glutamine	0.00	0.00	0.01	0.00
Inorganic Salts	0.00	0.00	0.27	0.00
Lactate	0.00	0.00	11.88	0.00
MAB	0.00	0.00	35.23	31.79
Other Media Components	0.00	0.00	0.00	0.00
Sodium Citrate	0.00	12.09	0.00	0.00
Vitamins	0.00	0.00	0.00	0.00
Water	0.00	0.00	30.08	0.00
WFI	11117.62	6702.00	1253.00	4447.05
TOTAL (kg/batch)	11184.73	6714.09	1332.33	4505.68
TOTAL (L/batch)	11154.57	6692.74	1326.73	4493.54

Stream Name	Waste-8	WFI-5	S-220	WFI-6
Source	P-36	INPUT	P-40	INPUT
Destination	OUTPUT	P-41	P-41	P-41
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	9.95	4.00	4.08	4.00
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	1002.73	1002.36	1002.67	1002.36
Component Flowrates (kg/batch)				
Amino Acids	0.03	0.00	0.00	0.00
Acetic-Acid	40.27	0.00	26.84	0.00
Dead Biomass	1.72	0.00	0.00	0.00
EDTA, Sodium	49.20	0.00	0.00	0.00
Glucose	0.11	0.00	0.00	0.00
Glutamine	0.01	0.00	0.00	0.00
Inorganic Salts	0.27	0.00	0.00	0.00
Lactate	11.88	0.00	0.00	0.00
MAB	3.43	0.00	31.79	0.00
Other Media Components	0.00	0.00	0.00	0.00
Sodium Chloride	24.60	0.00	0.00	0.00
Sodium Citrate	12.09	0.00	0.00	0.00
TRIS Base	24.60	0.00	0.00	0.00
TRIS HCl	73.81	0.00	0.00	0.00

Vitamins	0.00	0.00	0.00	0.00
Water	30.08	0.00	0.00	0.00
WFI	39055.46	1801.71	4447.05	501.18
TOTAL (kg/batch)	39327.56	1801.71	4505.68	501.18
TOTAL (L/batch)	39220.39	1797.47	4493.67	500.00

Stream Name	S-221	WFI-out	Waste-10	S-219
Source	P-41	P-41	P-41	P-39
Destination	P-40	OUTPUT	OUTPUT	P-40
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	4.35	4.00	4.35	4.07
Pressure (bar)	1.01	1.01	1.01	7.91
Density (g/L)	1002.28	1002.36	1002.51	1002.68
Component Flowrates (kg/batch)				
Acetic-Acid	0.71	0.00	26.14	26.84
Impurities	0.46	0.00	0.49	0.00
MAB	30.84	0.00	0.00	31.79
WFI	868.88	501.18	5379.87	4447.05
TOTAL (kg/batch)	900.89	501.18	5406.50	4505.68
TOTAL (L/batch)	898.85	500.00	5392.97	4493.66

Stream Name	Vent-8	S-222	S-202	S-203
Source	P-40	P-40	P-27	P-28
Destination	OUTPUT	P-42	P-28	P-29
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	4.17	4.35	25.02	25.00
Pressure (bar)	1.01	1.01	2.74	2.74
Density (g/L)	1.27	1002.28	996.54	996.57
Component Flowrates (kg/batch)				
Amino Acids	0.00	0.00	0.29	0.27
Acetic-Acid	0.00	0.71	0.00	0.00
Biomass	0.00	0.00	184.88	3.70
Dead Biomass	0.00	0.00	18.94	17.59
Glucose	0.00	0.00	1.23	1.14
Glutamine	0.00	0.00	0.14	0.13
Impurities	0.00	0.46	0.00	0.00
Inorganic Salts	0.00	0.00	2.98	2.77
Lactate	0.00	0.00	131.08	121.74
MAB	0.00	30.84	37.94	35.24
Nitrogen	4.91	0.00	0.00	0.00
Other Media Components	0.00	0.00	0.03	0.02
Oxygen	1.49	0.00	0.00	0.00
Vitamins	0.00	0.00	0.01	0.01

Water	0.00	0.00	331.88	308.24
WFI	0.00	868.88	13825.29	12840.42
TOTAL (kg/batch)	6.40	900.89	14534.70	13331.28
TOTAL (L/batch)	5047.79	898.85	14585.11	13377.12

Stream Name	Waste-5	S-206	Vent-7	S-207
Source	P-28	P-31	P-32	P-32
Destination	OUTPUT	P-32	OUTPUT	P-33
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.04	25.04	25.04
Pressure (bar)	1.01	6.18	1.01	1.01
Density (g/L)	996.29	996.56	1.18	996.56
Component Flowrates (kg/batch)				
Amino Acids	0.02	0.27	0.00	0.27
Biomass	181.19	0.00	0.00	0.00
Dead Biomass	1.35	17.59	0.00	17.59
Glucose	0.09	1.14	0.00	1.14
Glutamine	0.01	0.13	0.00	0.13
Inorganic Salts	0.21	2.77	0.00	2.77
Lactate	9.34	121.71	0.00	121.71
MAB	2.70	35.23	0.00	35.23
Nitrogen	0.00	0.00	12.10	0.00
Other Media Components	0.00	0.02	0.00	0.02
Oxygen	0.00	0.00	3.67	0.00
Vitamins	0.00	0.01	0.00	0.01
Water	23.64	308.16	0.00	308.16
WFI	984.87	12836.85	0.00	12836.85
TOTAL (kg/batch)	1203.42	13323.88	15.77	13323.88
TOTAL (L/batch)	1207.90	13369.86	13371.64	13369.86

Stream Name	S-217	S-218	S-204	S-205
Source	P-37	P-38	P-29	P-30
Destination	P-38	P-39	P-30	P-31
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	4.04	4.04	25.02	25.02
Pressure (bar)	4.46	4.46	4.46	4.46
Density (g/L)	1002.69	1002.69	996.57	996.57
Component Flowrates (kg/batch)				
Amino Acids	0.00	0.00	0.27	0.27
Acetic-Acid	26.84	26.84	0.00	0.00
Biomass	0.00	0.00	3.70	0.00
Dead Biomass	0.00	0.00	17.59	17.59
Glucose	0.00	0.00	1.14	1.14

Glutamine	0.00	0.00	0.13	0.13
Inorganic Salts	0.00	0.00	2.77	2.77
Lactate	0.00	0.00	121.74	121.71
MAB	31.79	31.79	35.24	35.23
Other Media Components	0.00	0.00	0.02	0.02
Vitamins	0.00	0.00	0.01	0.01
Water	0.00	0.00	308.24	308.16
WFI	4447.05	4447.05	12840.42	12836.85
TOTAL (kg/batch)	4505.68	4505.68	13331.28	13323.88
TOTAL (L/batch)	4493.60	4493.60	13377.21	13369.77

Stream Name	Waste-6	Polysorb80	S-223	Vent-9
Source	P-30	INPUT	P-42	P-43
Destination	OUTPUT	P-43	P-43	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.02	4.00	4.39	4.39
Pressure (bar)	4.46	1.01	4.46	1.01
Density (g/L)	995.63	881.61	1002.26	1.27
Component Flowrates (kg/batch)				
Amino Acids	0.00	0.00	0.00	0.00
Acetic-Acid	0.00	0.00	0.71	0.00
Biomass	3.70	0.00	0.00	0.00
Dead Biomass	0.01	0.00	0.00	0.00
Glucose	0.00	0.00	0.00	0.00
Glutamine	0.00	0.00	0.00	0.00
Impurities	0.00	0.00	0.46	0.00
Inorganic Salts	0.00	0.00	0.00	0.00
Lactate	0.03	0.00	0.00	0.00
MAB	0.01	0.00	30.84	0.00
Nitrogen	0.00	0.00	0.00	0.81
Other Media Components	0.00	0.00	0.00	0.00
Oxygen	0.00	0.00	0.00	0.25
Polysorbate 80	0.00	0.09	0.00	0.00
Vitamins	0.00	0.00	0.00	0.00
Water	0.09	0.00	0.00	0.00
WFI	3.57	0.09	868.88	0.00
TOTAL (kg/batch)	7.40	0.18	900.89	1.05
TOTAL (L/batch)	7.44	0.20	898.86	830.02

Stream Name	S-224	S-225	To IEX	S-208
Source	P-43	P-44	P-45	P-33
Destination	P-44	P-45	OUTPUT	P-34
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00

Temperature (°C)	4.39	4.43	4.43	25.05
Pressure (bar)	1.01	4.46	4.46	2.74
Density (g/L)	1002.23	1002.22	1002.22	996.55
Component Flowrates (kg/batch)				
Amino Acids	0.00	0.00	0.00	0.27
Acetic-Acid	0.71	0.71	0.71	0.00
Dead Biomass	0.00	0.00	0.00	17.59
Glucose	0.00	0.00	0.00	1.14
Glutamine	0.00	0.00	0.00	0.13
Impurities	0.46	0.46	0.46	0.00
Inorganic Salts	0.00	0.00	0.00	2.77
Lactate	0.00	0.00	0.00	121.71
MAB	30.84	30.84	30.84	35.23
Other Media Components	0.00	0.00	0.00	0.02
Polysorbate 80	0.09	0.09	0.09	0.00
Vitamins	0.00	0.00	0.00	0.01
Water	0.00	0.00	0.00	308.16
WFI	868.97	868.97	868.97	12836.85
TOTAL (kg/batch)	901.07	901.07	901.07	13323.88
TOTAL (L/batch)	899.06	899.07	899.07	13369.95

Stream Name	Waste-7	S-214
Source	P-34	P-34
Destination	OUTPUT	P-35
Stream Properties		
Activity (U/ml)	0.00	0.00
Temperature (°C)	4.00	4.00
Pressure (bar)	2.74	2.74
Density (g/L)	1004.30	1004.25
Component Flowrates (kg/batch)		
Amino Acids	0.24	0.03
Dead Biomass	15.87	1.72
Glucose	1.03	0.11
Glutamine	0.12	0.01
Inorganic Salts	2.50	0.27
Lactate	109.83	11.88
MAB	0.00	35.23
Other Media Components	0.02	0.00
Vitamins	0.01	0.00
Water	278.08	30.08
WFI	11583.85	1253.00
TOTAL (kg/batch)	11991.55	1332.33
TOTAL (L/batch)	11940.22	1326.69

3A. Pepsin CLEAVAGE OVERALL PROCESS DATA

Annual Operating Time	7915.92	h
Annual Throughput	0.00	kg MP
Batch Throughput	0.00	kg MP
Recipe Batch Time	28.88	h
Recipe Cycle Time	9.68	h
Number of Batches per Year	816.00	
MP = Main Product = Undefined		

STREAM DETAILS

Stream Name	From Bioreactor	S-201	S-206	Vent 7
Source	INPUT	P-26	P-31	P-32
Destination	P-26	P-27	P-32	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.04	25.04
Pressure (bar)	1.01	1.01	6.18	1.01
Density (g/L)	999.04	999.04	999.10	1.18
Component Flowrates (kg/batch)				
Amino Acids	3.49	3.49	3.15	0.00
Biomass	167.26	167.26	0.00	0.00
Dead Biomass	17.14	17.14	15.48	0.00
Glucose	14.75	14.75	13.32	0.00
Glutamine	1.71	1.71	1.54	0.00
Inorganic Salts	35.77	35.77	32.31	0.00
Lactate	118.59	118.59	107.12	0.00
MAB	34.32	34.32	31.00	0.00
Nitrogen	0.00	0.00	0.00	7.87
Other Media Components	0.31	0.31	0.28	0.00
Oxygen	0.00	0.00	0.00	2.39
Vitamins	0.15	0.15	0.13	0.00
Water	300.26	300.26	271.22	0.00
WFI	9096.99	9096.99	8217.36	0.00
TOTAL (kg/batch)	9790.72	9790.72	8692.92	10.26
TOTAL (L/batch)	9800.11	9800.11	8700.71	8701.88

Stream Name	S-207	From Dia1	S-208	Vent 8
Source	P-32	P-35	P-33	P-34
Destination	P-33	P-34	P-34	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00

Temperature (°C)	25.04	25.33	25.05	25.17
Pressure (bar)	1.01	1.01	2.74	1.01
Density (g/L)	999.10	995.33	999.10	1.18
Component Flowrates (kg/batch)				
Amino Acids	3.15	0.14	3.15	0.00
Dead Biomass	15.48	0.69	15.48	0.00
Glucose	13.32	0.60	13.32	0.00
Glutamine	1.54	0.07	1.54	0.00
HCl	0.00	0.00	0.00	0.00
Impurities	0.00	0.50	0.00	0.00
Inorganic Salts	32.31	1.45	32.31	0.00
Lactate	107.12	4.80	107.12	0.00
MAB	31.00	30.07	31.00	0.00
Nitrogen	0.00	0.00	0.00	10.50
Other Media Components	0.28	0.01	0.28	0.00
Oxygen	0.00	0.00	0.00	3.19
Sodium Acetate	0.00	6.70	0.00	0.00
Vitamins	0.13	0.01	0.13	0.00
Water	271.22	12.14	271.22	0.00
WFI	8217.36	2833.00	8217.36	0.00
TOTAL (kg/batch)	8692.92	2890.17	8692.92	13.69
TOTAL (L/batch)	8700.71	2903.75	8700.77	11617.11

Stream Name	To Dia1	S-209	Pepsin Dig Buffer 2- 1	WFI In 2-1
Source	P-34	P-34	INPUT	INPUT
Destination	P-35	P-36	P-35	P-35
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.05	25.33	25.00	4.00
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	999.10	995.98	995.37	1002.36
Component Flowrates (kg/batch)				
Amino Acids	3.15	0.14	0.00	0.00
Dead Biomass	15.48	0.69	0.00	0.00
Glucose	13.32	0.60	0.00	0.00
Glutamine	1.54	0.07	0.00	0.00
HCl	0.00	0.00	0.02	0.00
Impurities	0.00	0.50	0.00	0.00
Inorganic Salts	32.31	1.45	0.00	0.00
Lactate	107.12	4.80	0.00	0.00
MAB	31.00	30.07	0.00	0.00
Other Media Components	0.28	0.01	0.00	0.00
Sodium Acetate	0.00	6.70	46.99	0.00

Vitamins	0.13	0.01	0.00	0.00
Water	271.22	12.14	0.00	0.00
WFI	8217.36	2833.00	17274.02	1002.36
TOTAL (kg/batch)	8692.92	2890.17	17321.03	1002.36
TOTAL (L/batch)	8700.77	2901.84	17401.54	1000.00

Stream Name	WFI Out 2-1	Waste 7	S-202	S-203
Source	P-35	P-35	P-27	P-28
Destination	OUTPUT	OUTPUT	P-28	P-29
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	4.00	25.33	25.02	25.00
Pressure (bar)	1.01	1.01	2.74	2.74
Density (g/L)	1002.36	996.28	999.04	999.12
Component Flowrates (kg/batch)				
Amino Acids	0.00	3.01	3.49	3.15
Biomass	0.00	0.00	167.26	3.35
Dead Biomass	0.00	14.79	17.14	15.49
Glucose	0.00	12.73	14.75	13.33
Glutamine	0.00	1.47	1.71	1.54
HCl	0.00	0.02	0.00	0.00
Impurities	0.00	0.43	0.00	0.00
Inorganic Salts	0.00	30.87	35.77	32.33
Lactate	0.00	102.33	118.59	107.16
MAB	0.00	0.00	34.32	31.02
Other Media Components	0.00	0.27	0.31	0.28
Sodium Acetate	0.00	40.29	0.00	0.00
Vitamins	0.00	0.13	0.15	0.13
Water	0.00	259.08	300.26	271.33
WFI	1002.36	22658.39	9096.99	8220.54
TOTAL (kg/batch)	1002.36	23123.78	9790.72	8699.62
TOTAL (L/batch)	1000.00	23210.20	9800.18	8707.32

Stream Name	Waste 5	S-204	S-205	Waste 6
Source	P-28	P-29	P-30	P-30
Destination	OUTPUT	P-30	P-31	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.02	25.02	25.02
Pressure (bar)	2.74	4.46	4.46	4.46
Density (g/L)	998.45	999.11	999.11	996.90
Component Flowrates (kg/batch)				
Amino Acids	0.34	3.15	3.15	0.00
Biomass	163.92	3.35	0.00	3.35

Dead Biomass	1.65	15.49	15.48	0.01
Glucose	1.42	13.33	13.32	0.01
Glutamine	0.16	1.54	1.54	0.00
Inorganic Salts	3.45	32.33	32.31	0.01
Lactate	11.43	107.16	107.12	0.04
MAB	3.31	31.02	31.00	0.01
Other Media Components	0.03	0.28	0.28	0.00
Vitamins	0.01	0.13	0.13	0.00
Water	28.93	271.33	271.22	0.11
WFI	876.45	8220.54	8217.36	3.18
TOTAL (kg/batch)	1091.10	8699.62	8692.92	6.71
TOTAL (L/batch)	1092.79	8707.38	8700.66	6.73

Stream Name	S-210	Pepsin Dig Buffer 2- 2	Pepsin	Waste 8
Source	P-36	INPUT	INPUT	P-37
Destination	P-37	P-37	P-37	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.40	25.00	25.00	37.00
Pressure (bar)	7.91	1.01	1.01	10.54
Density (g/L)	995.95	995.37	994.70	990.33
Component Flowrates (kg/batch)				
Amino Acids	0.14	0.00	0.00	0.00
Dead Biomass	0.69	0.00	0.00	0.00
Glucose	0.60	0.00	0.00	0.00
Glutamine	0.07	0.00	0.00	0.00
HCl	0.00	0.00	0.00	0.00
Impurities	0.50	0.00	0.00	0.00
Inorganic Salts	1.45	0.00	0.00	0.00
Lactate	4.80	0.00	0.00	0.00
MAB	30.07	0.00	0.00	0.00
Other Media Components	0.01	0.00	0.00	0.00
Pepsin	0.00	0.00	1540.43	0.00
Sodium Acetate	6.70	4.18	0.00	0.00
Vitamins	0.01	0.00	0.00	0.00
Water	12.14	0.00	0.00	0.00
WFI	2833.00	1537.28	1540.43	3546.42
TOTAL (kg/batch)	2890.17	1541.46	3080.85	3546.42
TOTAL (L/batch)	2901.92	1548.63	3097.25	3581.05

Stream Name	S-211	S-212	Tris-HCl	Waste 9
Source	P-37	P-38	INPUT	P-39
Destination	P-38	P-39	P-39	OUTPUT

Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	37.00	37.26	4.00	28.89
Pressure (bar)	2.01	27.01	1.01	1.01
Density (g/L)	991.71	991.61	1096.65	1004.53
Component Flowrates (kg/batch)				
Amino Acids	0.14	0.14	0.00	0.01
Dead Biomass	0.69	0.69	0.00	0.04
F(ab') ₂	15.24	15.24	0.00	0.92
Glucose	0.60	0.60	0.00	0.04
Glutamine	0.07	0.07	0.00	0.00
Impurities	0.50	0.50	0.00	0.03
Inorganic Salts	1.45	1.45	0.00	0.09
Lactate	4.80	4.80	0.00	0.29
MAB	1.50	1.50	0.00	0.09
MAB Fc Fragments	13.33	13.33	0.00	0.81
Other Media Components	0.01	0.01	0.00	0.00
Pepsin	1540.43	1540.43	0.00	1540.43
Sodium Acetate	10.88	10.88	0.00	0.66
TRIS HCl	0.00	0.00	206.78	46.03
Vitamins	0.01	0.01	0.00	0.00
Water	12.14	12.14	0.00	0.74
WFI	2364.28	2364.28	2340.66	664.30
TOTAL (kg/batch)	3966.06	3966.06	2547.44	2254.47
TOTAL (L/batch)	3999.22	3999.61	2322.93	2244.31

Stream Name	S-213	RR Buffer 2- 1	S-220	WFI In 2-2
Source	P-39	INPUT	P-41	INPUT
Destination	P-40	P-42	P-42	P-42
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	26.81	4.00	26.89	4.00
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	1016.01	2084.92	1015.98	1002.36
Component Flowrates (kg/batch)				
Amino Acids	0.13	0.00	0.13	0.00
Dead Biomass	0.65	0.00	0.65	0.00
EDTA, Sodium	0.00	432.20	0.00	0.00
F(ab') ₂	14.31	0.00	14.31	0.00
Glucose	0.56	0.00	0.56	0.00
Glutamine	0.07	0.00	0.07	0.00
Impurities	0.47	0.00	0.47	0.00
Inorganic Salts	1.36	0.00	1.36	0.00

Lactate	4.51	0.00	4.51	0.00
MAB	1.41	0.00	1.41	0.00
MAb Fc Fragments	12.53	0.00	12.53	0.00
Other Media Components	0.01	0.00	0.01	0.00
Sodium Acetate	10.22	0.00	10.22	0.00
Sodium Chloride	0.00	12965.87	0.00	0.00
Sodium Phosphate	0.00	4082.05	0.00	0.00
TRIS HCl	160.75	0.00	160.75	0.00
Vitamins	0.01	0.00	0.01	0.00
Water	11.41	0.00	11.41	0.00
WFI	4040.65	0.00	4040.65	501.18
TOTAL (kg/batch)	4259.03	17480.11	4259.03	501.18
TOTAL (L/batch)	4191.93	8384.08	4192.04	500.00

Stream Name	S-219	WFI Out 2-2	Waste 10	S-214
Source	P-42	P-42	P-42	P-40
Destination	P-41	OUTPUT	OUTPUT	P-41
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	8.70	4.00	8.70	26.89
Pressure (bar)	1.01	1.01	1.01	7.91
Density (g/L)	1916.29	1002.36	1616.50	1015.98
Component Flowrates (kg/batch)				
Amino Acids	0.02	0.00	0.11	0.13
Dead Biomass	0.09	0.00	0.56	0.65
EDTA, Sodium	186.20	0.00	246.00	0.00
F(ab') ₂	14.31	0.00	0.00	14.31
Glucose	0.08	0.00	0.48	0.56
Glutamine	0.01	0.00	0.06	0.07
Impurities	0.34	0.00	0.17	0.47
Inorganic Salts	0.18	0.00	1.18	1.36
Lactate	0.61	0.00	3.90	4.51
MAB	0.19	0.00	1.19	1.41
MAb Fc Fragments	1.70	0.00	10.83	12.53
Other Media Components	0.00	0.00	0.01	0.01
Sodium Acetate	1.38	0.00	8.84	10.22
Sodium Chloride	5585.88	0.00	7379.99	0.00
Sodium Phosphate	1758.60	0.00	2323.44	0.00
TRIS HCl	21.76	0.00	138.99	160.75
Vitamins	0.00	0.00	0.01	0.01
Water	1.54	0.00	9.86	11.41
WFI	546.84	501.18	3493.81	4040.65
TOTAL (kg/batch)	8119.73	501.18	13619.41	4259.03
TOTAL (L/batch)	4237.21	500.00	8425.26	4192.04

Stream Name	Vent 11	S-215	S-216	2-MEA
Source	P-41	P-41	P-43	INPUT
Destination	OUTPUT	P-43	P-44	P-44
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	14.01	8.71	8.78	25.00
Pressure (bar)	1.01	1.01	7.91	1.01
Density (g/L)	1.22	1916.29	1916.26	994.70
Component Flowrates (kg/batch)				
2-MEA	0.00	0.00	0.00	0.08
Amino Acids	0.00	0.02	0.02	0.00
Dead Biomass	0.00	0.09	0.09	0.00
EDTA, Sodium	0.00	186.20	186.20	0.00
F(ab') ₂	0.00	14.31	14.31	0.00
Glucose	0.00	0.08	0.08	0.00
Glutamine	0.00	0.01	0.01	0.00
Impurities	0.00	0.34	0.34	0.00
Inorganic Salts	0.00	0.18	0.18	0.00
Lactate	0.00	0.61	0.61	0.00
MAB	0.00	0.19	0.19	0.00
MAb Fc Fragments	0.00	1.70	1.70	0.00
Nitrogen	8.22	0.00	0.00	0.00
Other Media Components	0.00	0.00	0.00	0.00
Oxygen	2.49	0.00	0.00	0.00
Sodium Acetate	0.00	1.38	1.38	0.00
Sodium Chloride	0.00	5585.88	5585.88	0.00
Sodium Phosphate	0.00	1758.60	1758.60	0.00
TRIS HCl	0.00	21.76	21.76	0.00
Vitamins	0.00	0.00	0.00	0.00
Water	0.00	1.54	1.54	0.00
WFI	0.00	546.84	546.84	0.00
TOTAL (kg/batch)	10.71	8119.73	8119.73	0.08
TOTAL (L/batch)	8748.17	4237.21	4237.28	0.08

Stream Name	S-217	WFI In 2-3	S-226	WFI In 2-4
Source	P-44	INPUT	P-46	INPUT
Destination	P-45	P-47	P-47	P-47
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	37.00	4.00	37.01	4.00
Pressure (bar)	10.54	1.01	1.01	1.01
Density (g/L)	1904.01	1002.36	1904.00	1002.36
Component Flowrates (kg/batch)				

2-MEA	0.08	0.00	0.08	0.00
Amino Acids	0.02	0.00	0.02	0.00
Dead Biomass	0.09	0.00	0.09	0.00
EDTA, Sodium	186.20	0.00	186.20	0.00
Glucose	0.08	0.00	0.08	0.00
Glutamine	0.01	0.00	0.01	0.00
Impurities	0.34	0.00	0.34	0.00
Inorganic Salts	0.18	0.00	0.18	0.00
Lactate	0.61	0.00	0.61	0.00
MAB	0.19	0.00	0.19	0.00
MAb Fab Fragments	14.31	0.00	14.31	0.00
MAb Fc Fragments	1.70	0.00	1.70	0.00
Other Media Components	0.00	0.00	0.00	0.00
Sodium Acetate	1.38	0.00	1.38	0.00
Sodium Chloride	5585.88	0.00	5585.88	0.00
Sodium Phosphate	1758.60	0.00	1758.60	0.00
TRIS HCl	21.76	0.00	21.76	0.00
Vitamins	0.00	0.00	0.00	0.00
Water	1.54	0.00	1.54	0.00
WFI	546.84	8549.31	546.84	501.18
TOTAL (kg/batch)	8119.81	8549.31	8119.81	501.18
TOTAL (L/batch)	4264.59	8529.19	4264.60	500.00

Stream Name	S-225	WFI Out 2-3	Waste 12	S-218
Source	P-47	P-47	P-47	P-45
Destination	P-46	OUTPUT	OUTPUT	P-46
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	20.30	4.00	20.30	37.01
Pressure (bar)	1.01	1.01	1.01	11.54
Density (g/L)	1119.19	1002.36	1389.74	1904.00
Component Flowrates (kg/batch)				
2-MEA	0.01	0.00	0.07	0.08
Amino Acids	0.00	0.00	0.02	0.02
Dead Biomass	0.01	0.00	0.08	0.09
EDTA, Sodium	25.20	0.00	161.00	186.20
Glucose	0.01	0.00	0.07	0.08
Glutamine	0.00	0.00	0.01	0.01
Impurities	0.23	0.00	0.12	0.34
Inorganic Salts	0.03	0.00	0.16	0.18
Lactate	0.08	0.00	0.53	0.61
MAB	0.02	0.00	0.16	0.19
MAb Fab Fragments	14.31	0.00	0.00	14.31
MAb Fc Fragments	0.23	0.00	1.47	1.70

Other Media Components	0.00	0.00	0.00	0.00
Sodium Acetate	0.19	0.00	1.20	1.38
Sodium Chloride	755.97	0.00	4829.92	5585.88
Sodium Phosphate	238.00	0.00	1520.60	1758.60
TRIS HCl	2.94	0.00	18.81	21.76
Vitamins	0.00	0.00	0.00	0.00
Water	0.21	0.00	1.34	1.54
WFI	3757.43	501.18	5338.72	546.84
TOTAL (kg/batch)	4794.89	501.18	11874.23	8119.81
TOTAL (L/batch)	4284.25	500.00	8544.24	4264.60

Stream Name	Vent 13	To Protein A
Source	P-46	P-46
Destination	OUTPUT	OUTPUT
Stream Properties		
Activity (U/ml)	0.00	0.00
Temperature (°C)	25.36	20.31
Pressure (bar)	1.01	1.01
Density (g/L)	1.18	1119.19
Component Flowrates (kg/batch)		
2-MEA	0.00	0.01
Amino Acids	0.00	0.00
Dead Biomass	0.00	0.01
EDTA, Sodium	0.00	25.20
Glucose	0.00	0.01
Glutamine	0.00	0.00
Impurities	0.00	0.23
Inorganic Salts	0.00	0.03
Lactate	0.00	0.08
MAB	0.00	0.02
MAb Fab Fragments	0.00	14.31
MAb Fc Fragments	0.00	0.23
Nitrogen	8.22	0.00
Other Media Components	0.00	0.00
Oxygen	2.50	0.00
Sodium Acetate	0.00	0.19
Sodium Chloride	0.00	755.97
Sodium Phosphate	0.00	238.00
TRIS HCl	0.00	2.94
Vitamins	0.00	0.00
Water	0.00	0.21
WFI	0.00	3757.43
TOTAL (kg/batch)	10.72	4794.89
TOTAL (L/batch)	9102.01	4284.25

3B. Pepsin CLEAVAGE OVERALL PROCESS DATA

Annual Operating Time	7874.21	h
Annual Throughput	100215.01	kg MP
Batch Throughput	879.08	kg MP
Recipe Batch Time	69.57	h
Recipe Cycle Time	69.07	h
Number of Batches per Year	114.00	
MP = Main Product = Total flow of stream To IEX		

STREAM DETAILS

Stream Name	From Pepsin Cleavage	S-101	ProtA- Equil.	ProtA- Wash
Source	INPUT	P-48	INPUT	INPUT
Destination	P-48	P-49	P-49	P-49
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	20.31	20.35	25.00	4.00
Pressure (bar)	1.01	4.46	1.01	1.01
Density (g/L)	1119.19	1119.17	998.35	1006.01
Component Flowrates (kg/batch)				
2-MEA	0.01	0.01	0.00	0.00
Amino Acids	0.00	0.00	0.00	0.00
Dead Biomass	0.01	0.01	0.00	0.00
EDTA, Sodium	25.20	25.20	0.17	0.20
Glucose	0.01	0.01	0.00	0.00
Glutamine	0.00	0.00	0.00	0.00
Impurities	0.23	0.23	0.00	0.00
Inorganic Salts	0.03	0.03	0.00	0.00
Lactate	0.08	0.08	0.00	0.00
MAB	0.02	0.02	0.00	0.00
MAB Fab Fragments	14.31	14.31	0.00	0.00
MAB Fc Fragments	0.23	0.23	0.00	0.00
Other Media Components	0.00	0.00	0.00	0.00
Sodium Acetate	0.19	0.19	0.00	0.00
Sodium Chloride	755.97	755.97	0.08	0.10
Sodium Phosphate	238.00	238.00	0.00	0.00
TRIS Base	0.00	0.00	0.08	0.10
TRIS HCl	2.94	2.94	0.25	0.31
Vitamins	0.00	0.00	0.00	0.00
Water	0.21	0.21	0.00	0.00
WFI	3757.43	3757.43	83.85	101.39

TOTAL (kg/batch)	4794.89	4794.89	84.44	102.11
TOTAL (L/batch)	4284.26	4284.31	84.58	101.50

Stream Name	ProtA-Elut.	ProtA-Reg.	S-227	Waste 13
Source	INPUT	INPUT	P-49	P-49
Destination	P-49	P-49	P-50	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	4.00	4.00	20.23	10.16
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	1002.70	1003.19	1118.26	1002.67
Component Flowrates (kg/batch)				
2-MEA	0.00	0.00	0.01	0.00
Amino Acids	0.00	0.00	0.00	0.00
Acetic-Acid	0.51	0.00	0.20	0.31
Dead Biomass	0.00	0.00	0.01	0.00
EDTA, Sodium	0.00	0.00	25.20	0.37
Glucose	0.00	0.00	0.01	0.00
Glutamine	0.00	0.00	0.00	0.00
Impurities	0.00	0.00	0.18	0.06
Inorganic Salts	0.00	0.00	0.03	0.00
Lactate	0.00	0.00	0.08	0.00
MAB	0.00	0.00	0.00	0.02
MAB Fab Fragments	0.00	0.00	14.31	0.00
MAB Fc Fragments	0.00	0.00	0.00	0.23
Other Media Components	0.00	0.00	0.00	0.00
Sodium Acetate	0.00	0.00	0.19	0.00
Sodium Chloride	0.00	0.00	755.97	0.19
Sodium Citrate	0.00	0.09	0.00	0.09
Sodium Phosphate	0.00	0.00	238.00	0.00
TRIS Base	0.00	0.00	0.00	0.19
TRIS HCl	0.00	0.00	2.94	0.56
Vitamins	0.00	0.00	0.00	0.00
Water	0.00	0.00	0.21	0.00
WFI	84.30	50.82	3791.15	286.64
TOTAL (kg/batch)	84.81	50.91	4828.50	288.65
TOTAL (L/batch)	84.58	50.75	4317.86	287.88

Stream Name	WFI 2-5	S-232	WFI 2-6	S-231
Source	INPUT	P-53	INPUT	P-54
Destination	P-54	P-54	P-54	P-53
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	4.00	20.30	4.00	16.29

Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	1002.36	1118.23	1002.36	1014.07
Component Flowrates (kg/batch)				
2-MEA	0.00	0.01	0.00	0.00
Amino Acids	0.00	0.00	0.00	0.00
Acetic-Acid	0.00	0.20	0.00	0.01
EDTA, Sodium	0.00	25.20	0.00	0.67
Glucose	0.00	0.01	0.00	0.00
Glutamine	0.00	0.00	0.00	0.00
Impurities	0.00	0.18	0.00	0.09
Inorganic Salts	0.00	0.03	0.00	0.00
Lactate	0.00	0.08	0.00	0.00
MAb Fab Fragments	0.00	14.31	0.00	14.31
Other Media Components	0.00	0.00	0.00	0.00
Sodium Acetate	0.00	0.19	0.00	0.01
Sodium Chloride	0.00	755.97	0.00	20.19
Sodium Phosphate	0.00	238.00	0.00	6.36
TRIS HCl	0.00	2.94	0.00	0.08
Vitamins	0.00	0.00	0.00	0.00
Water	0.00	0.21	0.00	0.01
WFI	1731.25	3791.14	501.18	837.19
TOTAL (kg/batch)	1731.25	4828.48	501.18	878.90
TOTAL (L/batch)	1727.18	4317.95	500.00	866.71

Stream Name	WFI Out 2-4	Waste 15	S-230	Vent 14
Source	P-54	P-54	P-52	P-53
Destination	OUTPUT	OUTPUT	P-53	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	4.00	16.29	20.30	19.12
Pressure (bar)	1.01	1.01	7.91	1.01
Density (g/L)	1002.36	1096.65	1118.24	1.20
Component Flowrates (kg/batch)				
2-MEA	0.00	0.01	0.01	0.00
Amino Acids	0.00	0.00	0.00	0.00
Acetic-Acid	0.00	0.20	0.20	0.00
EDTA, Sodium	0.00	24.53	25.20	0.00
Glucose	0.00	0.01	0.01	0.00
Glutamine	0.00	0.00	0.00	0.00
Impurities	0.00	0.09	0.18	0.00
Inorganic Salts	0.00	0.02	0.03	0.00
Lactate	0.00	0.08	0.08	0.00
MAb Fab Fragments	0.00	0.00	14.31	0.00
Nitrogen	0.00	0.00	0.00	4.65

Other Media Components	0.00	0.00	0.00	0.00
Oxygen	0.00	0.00	0.00	1.41
Sodium Acetate	0.00	0.18	0.19	0.00
Sodium Chloride	0.00	735.78	755.97	0.00
Sodium Phosphate	0.00	231.65	238.00	0.00
TRIS HCl	0.00	2.87	2.94	0.00
Vitamins	0.00	0.00	0.00	0.00
Water	0.00	0.20	0.21	0.00
WFI	501.18	4685.21	3791.14	0.00
TOTAL (kg/batch)	501.18	5680.83	4828.48	6.06
TOTAL (L/batch)	500.00	5180.17	4317.94	5034.34

Stream Name	S-233	S-228	S-229	Waste 14
Source	P-53	P-50	P-51	P-51
Destination	P-55	P-51	P-52	OUTPUT

Stream Properties

Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	16.30	20.27	20.27	20.27
Pressure (bar)	1.01	4.46	4.46	4.46
Density (g/L)	1014.07	1118.25	1118.25	1084.12

Component Flowrates (kg/batch)

2-MEA	0.00	0.01	0.01	0.00
Amino Acids	0.00	0.00	0.00	0.00
Acetic-Acid	0.01	0.20	0.20	0.00
Dead Biomass	0.00	0.01	0.00	0.01
EDTA, Sodium	0.67	25.20	25.20	0.00
Glucose	0.00	0.01	0.01	0.00
Glutamine	0.00	0.00	0.00	0.00
Impurities	0.09	0.18	0.18	0.00
Inorganic Salts	0.00	0.03	0.03	0.00
Lactate	0.00	0.08	0.08	0.00
MAb Fab Fragments	14.31	14.31	14.31	0.00
Other Media Components	0.00	0.00	0.00	0.00
Sodium Acetate	0.01	0.19	0.19	0.00
Sodium Chloride	20.19	755.97	755.97	0.00
Sodium Phosphate	6.36	238.00	238.00	0.00
TRIS HCl	0.08	2.94	2.94	0.00
Vitamins	0.00	0.00	0.00	0.00
Water	0.01	0.21	0.21	0.00
WFI	837.19	3791.15	3791.14	0.01
TOTAL (kg/batch)	878.90	4828.50	4828.48	0.03
TOTAL (L/batch)	866.71	4317.91	4317.89	0.02

Stream Name	Polysorb80	S-234	Vent 15	S-235
Source	INPUT	P-55	P-56	P-56

Destination	P-56	P-56	OUTPUT	P-57
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	4.00	16.34	16.34	16.34
Pressure (bar)	1.01	4.46	1.01	1.01
Density (g/L)	881.61	1014.06	1.21	1014.03
Component Flowrates (kg/batch)				
2-MEA	0.00	0.00	0.00	0.00
Amino Acids	0.00	0.00	0.00	0.00
Acetic-Acid	0.00	0.01	0.00	0.01
EDTA, Sodium	0.00	0.67	0.00	0.67
Glucose	0.00	0.00	0.00	0.00
Glutamine	0.00	0.00	0.00	0.00
Impurities	0.00	0.09	0.00	0.09
Inorganic Salts	0.00	0.00	0.00	0.00
Lactate	0.00	0.00	0.00	0.00
MAB Fab Fragments	0.00	14.31	0.00	14.31
Nitrogen	0.00	0.00	0.78	0.00
Other Media Components	0.00	0.00	0.00	0.00
Oxygen	0.00	0.00	0.24	0.00
Polysorbate 80	0.09	0.00	0.00	0.09
Sodium Acetate	0.00	0.01	0.00	0.01
Sodium Chloride	0.00	20.19	0.00	20.19
Sodium Phosphate	0.00	6.36	0.00	6.36
TRIS HCl	0.00	0.08	0.00	0.08
Vitamins	0.00	0.00	0.00	0.00
Water	0.00	0.01	0.00	0.01
WFI	0.09	837.19	0.00	837.28
TOTAL (kg/batch)	0.18	878.90	1.02	879.08
TOTAL (L/batch)	0.20	866.72	838.94	866.92

Stream Name	S-236	To IEX
Source	P-57	P-58
Destination	P-58	OUTPUT
Stream Properties		
Activity (U/ml)	0.00	0.00
Temperature (°C)	16.37	16.37
Pressure (bar)	4.46	4.46
Density (g/L)	1014.01	1014.01
Component Flowrates (kg/batch)		
2-MEA	0.00	0.00
Amino Acids	0.00	0.00
Acetic-Acid	0.01	0.01
EDTA, Sodium	0.67	0.67
Glucose	0.00	0.00

Glutamine	0.00	0.00
Impurities	0.09	0.09
Inorganic Salts	0.00	0.00
Lactate	0.00	0.00
MAB Fab Fragments	14.31	14.31
Other Media Components	0.00	0.00
Polysorbate 80	0.09	0.09
Sodium Acetate	0.01	0.01
Sodium Chloride	20.19	20.19
Sodium Phosphate	6.36	6.36
TRIS HCl	0.08	0.08
Vitamins	0.00	0.00
Water	0.01	0.01
WFI	837.28	837.28
TOTAL (kg/batch)	879.08	879.08
TOTAL (L/batch)	866.93	866.93

4. IEX OVERALL PROCESS DATA

Annual Operating Time	7916.33	h
Annual Throughput	11064.57	kg MP
Batch Throughput	14.31	kg MP
Recipe Batch Time	15.37	h
Recipe Cycle Time	10.23	h
Number of Batches per Year	773.00	

MP = Main Product = Flow of MAb Fab Fragments in stream From Protein A

STREAM DETAILS

Stream Name	Cat. Buffer B	Vent20	Cation Buffer A	Vent19
Source	INPUT	P-60	INPUT	P-59
Destination	P-60	OUTPUT	P-59	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	1046.15	1.18	994.70	1.18
Component Flowrates (kg/batch)				
MES	7.81	0.00	96.71	0.00
Nitrogen	0.00	0.76	0.00	9.01
Oxygen	0.00	0.23	0.00	2.74
Sodium Chloride	46.77	0.00	0.00	0.00
WFI	800.30	0.00	9810.13	0.00
TOTAL (kg/batch)	854.88	0.99	9906.84	11.75
TOTAL (L/batch)	817.17	836.58	9959.58	9959.58

Stream Name	Cat- Wash1	Cat- Load1	Cat- Equil2	Cat- Wash2
Source	P-59	P-59	P-66	P-65
Destination	P-65	P-62	P-68	P-68
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.01	25.01
Pressure (bar)	1.01	1.01	2.01	2.01
Density (g/L)	994.70	994.70	994.70	994.70
Component Flowrates (kg/batch)				
MES	4.55	87.60	4.55	4.55
WFI	461.86	8886.41	461.86	461.86
TOTAL (kg/batch)	466.42	8974.01	466.42	466.42
TOTAL (L/batch)	468.90	9021.79	468.90	468.90

Stream Name	Cat-WFI	Cat-Elute2	Cat-Strip2	Fab Load
Source	INPUT	P-64	P-63	P-67
Destination	P-68	P-68	P-68	P-68
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.01	25.01	24.25
Pressure (bar)	1.01	2.01	2.01	2.01
Density (g/L)	994.70	1021.87	1021.87	996.40
Component Flowrates (kg/batch)				
2-MEA	0.00	0.00	0.00	0.00
Amino Acids	0.00	0.00	0.00	0.00
Acetic-Acid	0.00	0.00	0.00	0.01
EDTA, Sodium	0.00	0.00	0.00	0.67
Glucose	0.00	0.00	0.00	0.00
Glutamine	0.00	0.00	0.00	0.00
Impurities	0.00	0.00	0.00	0.09
Inorganic Salts	0.00	0.00	0.00	0.00
Lactate	0.00	0.00	0.00	0.00
MAb Fab Fragments	0.00	0.00	0.00	14.31
MES	0.00	3.43	4.38	87.60
Other Media Components	0.00	0.00	0.00	0.00
Polysorbate 80	0.00	0.00	0.00	0.09
Sodium Acetate	0.00	0.00	0.00	0.01
Sodium Chloride	0.00	20.56	26.21	20.19
Sodium Phosphate	0.00	0.00	0.00	6.36
TRIS HCl	0.00	0.00	0.00	0.08
Vitamins	0.00	0.00	0.00	0.00
Water	0.00	0.00	0.00	0.01
WFI	1033.52	351.74	448.56	9723.68
TOTAL (kg/batch)	1033.52	375.72	479.16	9853.09
TOTAL (L/batch)	1039.02	367.68	468.90	9888.68
Stream Name	S-302	Waste 17	From Protein A	Anion Buffer A
Source	P-68	P-68	INPUT	INPUT
Destination	P-69	OUTPUT	P-61	P-77
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	24.95	24.41	16.37	25.00
Pressure (bar)	1.01	1.01	4.46	1.01
Density (g/L)	1001.36	997.76	1014.04	1002.00
Component Flowrates (kg/batch)				
2-MEA	0.00	0.00	0.00	0.00
Amino Acids	0.00	0.00	0.00	0.00
Acetic-Acid	0.00	0.01	0.01	0.00

EDTA, Sodium	0.00	0.67	0.67	0.00
Glucose	0.00	0.00	0.00	0.00
Glutamine	0.00	0.00	0.00	0.00
Impurities	0.01	0.08	0.09	0.00
Inorganic Salts	0.00	0.00	0.00	0.00
Lactate	0.00	0.00	0.00	0.00
MAb Fab Fragments	12.92	1.40	14.31	0.00
MES	0.46	104.06	0.00	0.00
Other Media Components	0.00	0.00	0.00	0.00
Polysorbate 80	0.00	0.09	0.09	0.00
Sodium Acetate	0.00	0.01	0.01	0.00
Sodium Chloride	2.74	64.22	20.19	9.75
Sodium Phosphate	0.00	6.36	6.36	0.00
TRIS Base	0.00	0.00	0.00	16.47
TRIS HCl	0.00	0.08	0.08	0.00
Vitamins	0.00	0.00	0.00	0.00
Water	0.00	0.01	0.01	0.00
WFI	184.70	12296.52	837.28	3872.46
TOTAL (kg/batch)	200.83	12473.49	879.08	3898.68
TOTAL (L/batch)	200.55	12501.54	866.91	3890.91

Stream Name	Vent21	Anion-Load1	Anion-Wash1	Anion-Load2
Source	P-77	P-77	P-77	P-73
Destination	OUTPUT	P-73	P-74	P-69
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.01
Pressure (bar)	1.01	1.01	1.01	2.01
Density (g/L)	1.18	998.20	998.20	998.19
Component Flowrates (kg/batch)				
Nitrogen	3.53	0.00	0.00	0.00
Oxygen	1.07	0.00	0.00	0.00
Sodium Chloride	0.00	8.73	0.29	8.73
TRIS Base	0.00	14.76	0.49	14.76
WFI	0.00	3470.18	114.94	3470.18
TOTAL (kg/batch)	4.61	3493.67	115.72	3493.67
TOTAL (L/batch)	3905.72	3499.99	115.92	3500.00

Stream Name	Vent17	S-303	S-304	Anion-Equil2
Source	P-69	P-69	P-70	P-75
Destination	OUTPUT	P-70	P-71	P-71
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.01	25.01	25.02	25.01

Pressure (bar)	1.01	1.01	2.01	2.01
Density (g/L)	1.18	998.36	998.36	998.19
Component Flowrates (kg/batch)				
Impurities	0.00	0.01	0.01	0.00
MAb Fab Fragments	0.00	12.92	12.92	0.00
MES	0.00	0.46	0.46	0.00
Nitrogen	3.35	0.00	0.00	0.00
Oxygen	1.02	0.00	0.00	0.00
Sodium Chloride	0.00	11.48	11.48	0.72
TRIS Base	0.00	14.76	14.76	1.22
WFI	0.00	3654.88	3654.88	287.34
TOTAL (kg/batch)	4.36	3694.50	3694.50	289.29
TOTAL (L/batch)	3700.65	3700.55	3700.57	289.81

Stream Name	Anion-Wash2	Anion-Strip2	S-305	Waste 18
Source	P-74	P-76	P-71	P-71
Destination	P-71	P-71	P-72	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.01	25.01	25.02	25.01
Pressure (bar)	2.01	2.01	1.01	2.01
Density (g/L)	998.19	1024.67	998.36	1014.48
Component Flowrates (kg/batch)				
Impurities	0.00	0.00	0.00	0.01
MAb Fab Fragments	0.00	0.00	12.89	0.03
MES	0.00	0.00	0.46	0.00
Sodium Chloride	0.29	26.11	11.76	26.83
TRIS Base	0.49	2.23	15.25	3.46
WFI	114.94	446.79	3769.82	734.14
TOTAL (kg/batch)	115.72	475.14	3810.17	764.47
TOTAL (L/batch)	115.93	463.70	3816.45	753.55

Stream Name	Vent18	S-306	To PEG	Anion Buffer B
Source	P-72	P-72	P-79	INPUT
Destination	OUTPUT	P-79	OUTPUT	P-78
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.02	25.02	25.03	25.00
Pressure (bar)	1.01	1.01	2.01	1.01
Density (g/L)	1.18	998.36	998.35	1051.88
Component Flowrates (kg/batch)				
Impurities	0.00	0.00	0.00	0.00
MAb Fab Fragments	0.00	12.89	12.89	0.00
MES	0.00	0.46	0.46	0.00

Nitrogen	3.45	0.00	0.00	0.00
Oxygen	1.05	0.00	0.00	0.00
Sodium Chloride	0.00	11.76	11.76	26.11
TRIS Base	0.00	15.25	15.25	2.23
WFI	0.00	3769.82	3769.82	446.79
TOTAL (kg/batch)	4.50	3810.17	3810.17	475.14
TOTAL (L/batch)	3816.70	3816.45	3816.47	451.70

Stream Name	Vent16
Source	P-78
Destination	OUTPUT
Stream Properties	
Activity (U/ml)	0.00
Temperature (°C)	25.00
Pressure (bar)	1.01
Density (g/L)	1.18
Component Flowrates (kg/batch)	
Nitrogen	0.42
Oxygen	0.13
TOTAL (kg/batch)	0.55
TOTAL (L/batch)	463.70

5. PEGylation OVERALL PROCESS DATA

Annual Operating Time	7919.92	h
Annual Throughput	0.00	kg MP
Batch Throughput	0.00	kg MP
Recipe Batch Time	13.28	h
Recipe Cycle Time	12.37	h
Number of Batches per Year	640.00	
MP = Main Product = Undefined		

STREAM DETAILS

Stream Name	From Dia1	S-401	Vent 22	To Dia1
Source	P-81	INPUT	P-80	P-80
Destination	P-80	P-80	OUTPUT	P-81
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	11.29	25.03	11.30	25.03
Pressure (bar)	1.01	2.01	1.01	1.01
Density (g/L)	1000.51	998.35	1.24	998.35
Component Flowrates (kg/batch)				
EDTA, Sodium	0.93	0.00	0.00	0.00
Impurities	0.00	0.00	0.00	0.00
MAb Fab Fragments	12.89	12.89	0.00	12.89
MES	0.02	0.46	0.00	0.46
Nitrogen	0.00	0.00	1.21	0.00
Oxygen	0.00	0.00	0.37	0.00
Phosphate	11.86	0.00	0.00	0.00
Sodium Chloride	0.61	11.76	0.00	11.76
TRIS Base	0.79	15.25	0.00	15.25
WFI	1444.33	3769.82	0.00	3769.82
TOTAL (kg/batch)	1471.43	3810.17	1.58	3810.17
TOTAL (L/batch)	1470.68	3816.47	1275.85	3816.47

Stream Name	S-402	RR Buffer 4- 1	WFI In 4-1	WFI Out 4- 1
Source	P-80	INPUT	INPUT	P-81
Destination	P-82	P-81	P-81	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	11.30	4.00	4.00	4.00
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	1000.50	1003.09	1002.36	1002.36
Component Flowrates (kg/batch)				

EDTA, Sodium	0.93	5.64	0.00	0.00
Impurities	0.00	0.00	0.00	0.00
MAb Fab Fragments	12.89	0.00	0.00	0.00
MES	0.02	0.00	0.00	0.00
Phosphate	11.86	71.98	0.00	0.00
Sodium Chloride	0.61	0.00	0.00	0.00
TRIS Base	0.79	0.00	0.00	0.00
WFI	1444.33	7578.93	1503.54	1503.54
TOTAL (kg/batch)	1471.43	7656.55	1503.54	1503.54
TOTAL (L/batch)	1470.69	7632.93	1500.00	1500.00

Stream Name	Waste 19	S-403	2-MEA	S-404
Source	P-81	P-82	INPUT	P-83
Destination	OUTPUT	P-83	P-83	P-84
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	11.29	11.31	25.00	37.00
Pressure (bar)	1.01	2.01	1.01	10.54
Density (g/L)	1001.26	1000.50	994.70	991.13
Component Flowrates (kg/batch)				
2-MEA	0.00	0.00	8.90	8.90
EDTA, Sodium	4.71	0.93	0.00	0.93
Impurities	0.00	0.00	0.00	0.00
MAb Fab Fragments	0.00	12.89	0.00	0.64
MES	0.43	0.02	0.00	0.02
Phosphate	60.11	11.86	0.00	11.86
Reduced MAb Fab Fragments	0.00	0.00	0.00	12.24
Sodium Chloride	11.16	0.61	0.00	0.61
TRIS Base	14.46	0.79	0.00	0.79
WFI	9904.42	1444.33	0.00	1444.33
TOTAL (kg/batch)	9995.29	1471.43	8.90	1480.33
TOTAL (L/batch)	9982.72	1470.69	8.95	1493.58

Stream Name	S-405	From Dia2	Vent 24	To Dia2
Source	P-84	P-86	P-85	P-85
Destination	P-85	P-85	OUTPUT	P-86
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	37.01	15.15	20.89	37.01
Pressure (bar)	11.54	1.01	1.01	1.01
Density (g/L)	991.13	998.72	1.20	991.13
Component Flowrates (kg/batch)				
2-MEA	8.90	1.21	0.00	8.90
EDTA Disodium	0.00	0.95	0.00	0.00

EDTA, Sodium	0.93	0.13	0.00	0.93
Impurities	0.00	0.00	0.00	0.00
MAb Fab Fragments	0.64	0.64	0.00	0.64
MES	0.02	0.00	0.00	0.02
Nitrogen	0.00	0.00	2.65	0.00
Oxygen	0.00	0.00	0.80	0.00
Phosphate	11.86	13.68	0.00	11.86
Reduced MAb Fab Fragments	12.24	12.24	0.00	12.24
Sodium Chloride	0.61	0.08	0.00	0.61
TRIS Base	0.79	0.11	0.00	0.79
WFI	1444.33	1466.61	0.00	1444.33
TOTAL (kg/batch)	1480.33	1495.64	3.45	1480.33
TOTAL (L/batch)	1493.58	1497.56	2887.31	1493.58

Stream Name	S-406	PR Buffer 4- 1	WFI In 4-2	WFI Out 4- 2
Source	P-85	INPUT	INPUT	P-86
Destination	P-87	P-86	P-86	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	15.15	4.00	4.00	4.00
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	998.72	1003.09	1002.36	1002.36
Component Flowrates (kg/batch)				
2-MEA	1.21	0.00	0.00	0.00
EDTA Disodium	0.95	2.21	0.00	0.00
EDTA, Sodium	0.13	0.00	0.00	0.00
Impurities	0.00	0.00	0.00	0.00
MAb Fab Fragments	0.64	0.00	0.00	0.00
MES	0.00	0.00	0.00	0.00
Phosphate	13.68	28.17	0.00	0.00
Reduced MAb Fab Fragments	12.24	0.00	0.00	0.00
Sodium Chloride	0.08	0.00	0.00	0.00
TRIS Base	0.11	0.00	0.00	0.00
WFI	1466.61	2966.03	501.18	501.18
TOTAL (kg/batch)	1495.64	2996.40	501.18	501.18
TOTAL (L/batch)	1497.56	2987.16	500.00	500.00

Stream Name	Waste 21	S-407	PEG	Waste 22
Source	P-86	P-87	INPUT	P-88
Destination	OUTPUT	P-88	P-88	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	15.15	15.16	25.00	37.00

Pressure (bar)	1.01	2.01	1.01	10.54
Density (g/L)	998.85	998.71	994.70	990.33
Component Flowrates (kg/batch)				
2-MEA	7.70	1.21	0.00	0.00
EDTA Disodium	1.26	0.95	0.00	0.00
EDTA, Sodium	0.80	0.13	0.00	0.00
Impurities	0.00	0.00	0.00	0.00
MAb Fab Fragments	0.00	0.64	0.00	0.00
MES	0.02	0.00	0.00	0.00
PEG	0.00	0.00	225.48	0.00
Phosphate	26.35	13.68	0.00	0.00
Reduced MAb Fab Fragments	0.00	12.24	0.00	0.00
Sodium Chloride	0.53	0.08	0.00	0.00
TRIS Base	0.68	0.11	0.00	0.00
WFI	2943.75	1466.61	0.00	879.96
TOTAL (kg/batch)	2981.09	1495.64	225.48	879.96
TOTAL (L/batch)	2984.52	1497.57	226.68	888.56

Stream Name	S-408	S-409	From Dia3	Vent 26
Source	P-88	P-89	P-91	P-90
Destination	P-89	P-90	P-90	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	37.00	37.01	15.18	20.92
Pressure (bar)	1.88	2.88	1.01	1.01
Density (g/L)	991.08	991.08	998.39	1.20
Component Flowrates (kg/batch)				
2-MEA	1.21	1.21	0.16	0.00
EDTA Disodium	0.95	0.95	0.13	0.00
EDTA, Sodium	0.13	0.13	0.02	0.00
Impurities	0.00	0.00	0.00	0.00
MAb Fab Fragments	0.64	0.64	0.09	0.00
MES	0.00	0.00	0.00	0.00
Nitrogen	0.00	0.00	0.00	1.51
Oxygen	0.00	0.00	0.00	0.46
PEG	216.17	216.17	29.26	0.00
PEGylated MAb F	20.93	20.93	20.93	0.00
Phosphate	13.68	13.68	1.85	0.00
Reduced MAb Fab Fragments	0.61	0.61	0.08	0.00
Sodium Chloride	0.08	0.08	0.01	0.00
TRIS Base	0.11	0.11	0.01	0.00
WFI	586.64	586.64	796.66	0.00
TOTAL (kg/batch)	841.15	841.15	849.21	1.96
TOTAL (L/batch)	848.72	848.72	850.58	1640.44

Stream Name	To Dia3	S-410	WFI In 4-4	WFI In 4-3
Source	P-90	P-90	INPUT	INPUT
Destination	P-91	P-94	P-91	P-91
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	37.01	15.18	4.00	4.00
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	991.08	998.38	1002.36	1002.36
Component Flowrates (kg/batch)				
2-MEA	1.21	0.16	0.00	0.00
EDTA Disodium	0.95	0.13	0.00	0.00
EDTA, Sodium	0.13	0.02	0.00	0.00
Impurities	0.00	0.00	0.00	0.00
MAb Fab Fragments	0.64	0.09	0.00	0.00
MES	0.00	0.00	0.00	0.00
PEG	216.17	29.26	0.00	0.00
PEGylated MAb F	20.93	20.93	0.00	0.00
Phosphate	13.68	1.85	0.00	0.00
Reduced MAb Fab Fragments	0.61	0.08	0.00	0.00
Sodium Chloride	0.08	0.01	0.00	0.00
TRIS Base	0.11	0.01	0.00	0.00
WFI	586.64	796.66	1701.44	501.18
TOTAL (kg/batch)	841.15	849.21	1701.44	501.18
TOTAL (L/batch)	848.72	850.58	1697.44	500.00

Stream Name	WFI Out 4-3	Waste 23	Cation Buffer 1	Load1
Source	P-91	P-91	INPUT	P-93
Destination	OUTPUT	OUTPUT	P-93	P-95
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	4.00	15.18	25.00	25.00
Pressure (bar)	1.01	1.01	1.01	3.70
Density (g/L)	1002.36	998.61	994.70	994.70
Component Flowrates (kg/batch)				
2-MEA	0.00	1.04	0.00	0.00
EDTA Disodium	0.00	0.82	0.00	0.00
EDTA, Sodium	0.00	0.11	0.00	0.00
Impurities	0.00	0.00	0.00	0.00
MAb Fab Fragments	0.00	0.56	0.00	0.00
MES	0.00	0.00	0.00	0.00
PEG	0.00	186.92	0.00	0.00
Phosphate	0.00	11.83	6.46	3.96
Reduced MAb Fab Fragments	0.00	0.53	0.00	0.00

Sodium Chloride	0.00	0.07	0.00	0.00
TRIS Base	0.00	0.09	0.00	0.00
Water	0.00	0.00	3401.45	2084.92
WFI	501.18	1491.42	0.00	0.00
TOTAL (kg/batch)	501.18	1693.39	3407.91	2088.88
TOTAL (L/batch)	500.00	1695.75	3426.05	2100.00

Stream Name	Cation Buffer 2	Equil2	Wash2	WFI In 4-5
Source	INPUT	P-99	P-98	INPUT
Destination	P-92	P-101	P-101	P-101
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.01	25.01	25.00
Pressure (bar)	1.01	11.13	2.23	1.01
Density (g/L)	1046.58	994.70	994.70	994.70
Component Flowrates (kg/batch)				
Phosphate	2.99	1.25	1.25	0.00
Sodium Chloride	92.09	0.00	0.00	0.00
Water	0.00	658.27	658.27	0.00
WFI	1574.12	0.00	0.00	1013.62
TOTAL (kg/batch)	1669.20	659.52	659.52	1013.62
TOTAL (L/batch)	1594.91	663.03	663.03	1019.01

Stream Name	Cat- Elute2	Cat-Strip	Load	Final Formulation
Source	P-97	P-96	P-100	P-101
Destination	P-101	P-101	P-101	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.01	25.01	22.30	24.90
Pressure (bar)	11.13	2.60	2.01	1.01
Density (g/L)	1022.10	1022.10	995.72	1007.21
Component Flowrates (kg/batch)				
2-MEA	0.00	0.00	0.16	0.00
EDTA Disodium	0.00	0.00	0.13	0.00
EDTA, Sodium	0.00	0.00	0.02	0.00
Impurities	0.00	0.00	0.00	0.00
MAb Fab Fragments	0.00	0.00	0.09	0.00
MES	0.00	0.00	0.00	0.00
PEG	0.00	0.00	29.26	0.00
PEGylated MAb F	0.00	0.00	20.93	18.89
Phosphate	1.78	1.21	5.81	0.24
Reduced MAb Fab Fragments	0.00	0.00	0.08	0.00
Sodium Chloride	54.70	37.39	0.01	7.29
TRIS Base	0.00	0.00	0.01	0.00

Water	0.00	0.00	2084.92	0.00
WFI	935.04	639.08	796.66	259.82
TOTAL (kg/batch)	991.52	677.68	2938.09	286.24
TOTAL (L/batch)	970.08	663.03	2950.72	284.19

Stream Name	Waste 24
Source	P-101
Destination	OUTPUT

Stream Properties

Activity (U/ml)	0.00
Temperature (°C)	24.09
Pressure (bar)	1.01
Density (g/L)	999.79

Component Flowrates (kg/batch)

2-MEA	0.16
EDTA Disodium	0.13
EDTA, Sodium	0.02
Impurities	0.00
MAb Fab Fragments	0.09
MacroCap SP	2026.87
MES	0.00
PEG	29.26
PEGylated MAb F	2.04
Phosphate	11.07
Reduced MAb Fab Fragments	0.08
Sodium Chloride	84.80
TRIS Base	0.01
Water	3401.45
WFI	3124.58
TOTAL (kg/batch)	8680.56
TOTAL (L/batch)	8682.37

6. Final Formulation OVERALL PROCESS DATA

Annual Operating Time	7914.09	h
Annual Throughput	0.00	kg MP
Batch Throughput	0.00	kg MP
Recipe Batch Time	14.76	h
Recipe Cycle Time	11.33	h
Number of Batches per Year	698.00	
MP = Main Product = Undefined		

STREAM DETAILS

Stream Name	From PEG	S-501	S-508	Vent-29
Source	INPUT	P-102	P-104	P-103
Destination	P-102	P-103	P-103	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	24.90	24.92	25.22	25.11
Pressure (bar)	1.01	2.51	1.01	1.01
Density (g/L)	1007.21	1007.21	999.63	1.18
Component Flowrates (kg/batch)				
Impurities	0.00	0.00	0.00	0.00
KCl	0.00	0.00	0.00	0.00
KH ₂ PO ₄	0.00	0.00	0.00	0.00
MAb Fab Fragments	0.00	0.00	0.00	0.00
Na ₂ HPO ₄	0.00	0.00	0.16	0.00
Nitrogen	0.00	0.00	0.00	0.43
Oxygen	0.00	0.00	0.00	0.13
PEGylated MAb F	18.89	18.89	18.42	0.00
Phosphate	0.24	0.24	0.02	0.00
Sodium Chloride	7.29	7.29	1.82	0.00
WFI	259.82	259.82	168.99	0.00
TOTAL (kg/batch)	286.24	286.24	189.41	0.56
TOTAL (L/batch)	284.19	284.20	189.48	474.02

Stream Name	S-507	S-502	PBS	Dia-WFI
Source	P-103	P-103	INPUT	INPUT
Destination	P-104	P-105	P-104	P-104
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	24.92	25.22	25.00	25.00
Pressure (bar)	1.01	1.01	1.01	1.01
Density (g/L)	1007.21	999.63	999.04	994.70
Component Flowrates (kg/batch)				

Impurities	0.00	0.00	0.00	0.00
KCl	0.00	0.00	0.00	0.00
KH ₂ PO ₄	0.00	0.00	0.00	0.00
MAb Fab Fragments	0.00	0.00	0.00	0.00
Na ₂ HPO ₄	0.00	0.16	0.42	0.00
PEGylated MAb F	18.89	18.42	0.00	0.00
Phosphate	0.24	0.02	0.00	0.00
Sodium Chloride	7.29	1.82	3.03	0.00
WFI	259.82	168.99	375.12	497.35
TOTAL (kg/batch)	286.24	189.41	378.56	497.35
TOTAL (L/batch)	284.20	189.48	378.93	500.00

Stream Name	Waste-25	Waste-26	S-503	S-504
Source	P-104	P-104	P-105	P-106
Destination	OUTPUT	OUTPUT	P-106	P-107
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.22	25.27	25.27
Pressure (bar)	1.01	1.01	5.15	5.15
Density (g/L)	994.70	1003.57	999.62	999.62
Component Flowrates (kg/batch)				
Impurities	0.00	0.00	0.00	0.00
KCl	0.00	0.00	0.00	0.00
KH ₂ PO ₄	0.00	0.00	0.00	0.00
MAb Fab Fragments	0.00	0.00	0.00	0.00
Na ₂ HPO ₄	0.00	0.25	0.16	0.16
PEGylated MAb F	0.00	0.00	18.42	18.24
Phosphate	0.00	0.22	0.02	0.02
Sodium Chloride	0.00	8.51	1.82	1.81
WFI	497.35	466.42	168.99	168.81
TOTAL (kg/batch)	497.35	475.40	189.41	189.04
TOTAL (L/batch)	500.00	473.70	189.48	189.11

Stream Name	Waste-27	S-505	Waste-28	S-506
Source	P-106	P-107	P-107	P-108
Destination	OUTPUT	P-108	OUTPUT	P-109
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.27	25.27	25.27	25.27
Pressure (bar)	5.15	5.15	5.15	1.24
Density (g/L)	997.38	999.63	997.38	999.63
Component Flowrates (kg/batch)				
Impurities	0.00	0.00	0.00	0.00
KCl	0.00	0.00	0.00	0.00
KH ₂ PO ₄	0.00	0.00	0.00	0.00

MAb Fab Fragments	0.00	0.00	0.00	0.00
Na2HPO4	0.00	0.16	0.00	0.16
PEGylated MAb F	0.18	18.05	0.18	18.05
Phosphate	0.00	0.02	0.00	0.02
Sodium Chloride	0.00	1.81	0.00	1.81
WFI	0.18	168.63	0.18	168.63
TOTAL (kg/batch)	0.37	188.68	0.37	188.68
TOTAL (L/batch)	0.37	188.75	0.37	188.75

Stream Name	Final Product
Source	P-109
Destination	OUTPUT
Stream Properties	
Activity (U/ml)	0.00
Temperature (°C)	- 80.00
Pressure (bar)	1.24
Density (g/L)	1038.11
Component Flowrates (kg/batch)	
Impurities	0.00
KCl	0.00
KH2PO4	0.00
MAb Fab Fragments	0.00
Na2HPO4	0.16
PEGylated MAb F	18.05
Phosphate	0.02
Sodium Chloride	1.81
WFI	168.63
TOTAL (kg/batch)	188.68
TOTAL (L/batch)	181.75

Appendix E – SuperPro Validation Calculations

Unit: P-1/TFR-101

T-Flask

Process Description:

Non-treated, sterile flasks for the suspension and growth of cell cultures.

Inlet Components (kg/batch)		Main Components		
		Outlet Components (kg/batch)	Theoretical	SuperPro
AAs	0.00267	AAs	0.00262	0.00262
Glucose	0.01132	Biomass	0.00031	0.00031
Glutamine	0.00131	DeadBiomass	0.00003	0.00003
Inorganic Salts	0.02742	Glucose	0.01042	0.01109
OtherMedia	0.00024	Glutamine	0.00129	0.00128
Vitamins	0.00011	Inorganic Salts	0.02218	0.02686
WFI	2.11021	Lactate	0.00021	0.00021
TOTAL	2.15309	MAB	0.00006	0.00006
		OtherMedia	0.00024	0.00023
		Vitamins	0.00011	0.00011
		Water	0.00053	0.00053
		WFI	2.11021	2.11021
		TOTAL	2.14822	2.15354

Reaction Extent: 70%

EQUATION

REACTANTS

Components	Mass Coeff %
AAs	6.21
Glucose	26.28
Glutamine	3.04
Inorganic Salts	63.66
OtherMedia	0.55
Oxygen	100
Vitamins	0.26

Total **200**

PRODUCTS

Components	Mass Coeff %
Biomass	34.26
Carb. Dioxide	69.41
DeadBiomass	3.51
MAB	7.03
Water	61.5
Lactate	24.29

200
Unit: P-2/RBR-101

Roller Bottle

Process Description:

Non-treated, sterile bottles for the suspension and growth of cell cultures.

Inlet Components (kg/batch)		Main Components		
		Outlet Components (kg/batch)	Theoretical	SuperPro
AAs	0.01363	AAs	0.01338	0.01334
Biomass	0.00031	Biomass	0.00187	0.00189
DeadBiomass	0.00003	DeadBiomass	0.00018	0.00019
Glucose	0.05771	Glucose	0.05651	0.05647
Glutamine	0.00667	Glutamine	0.00652	0.00653
Inorganic Salts	0.13976	Inorganic Salts	0.13692	0.1368
Lactate	0.00021	Lactate	0.00134	0.00134
MAB	0.00006	MAB	0.00397	0.00039
OtherMedia	0.00121	OtherMedia	0.00118	0.00118
Vitamins	0.00057	Vitamins	0.00055	0.00056
Water	0.00053	Water	0.00338	0.00339
WFI	10.80021	WFI	10.79991	10.79991
TOTAL (kg/batch)	11.02088		11.02571	11.02199

Reaction Extent: 70%

EQUATION

REACTANTS

Components	Mass Coeff %
AAs	6.21
Glucose	26.28
Glutamine	3.04
Inorganic Salts	63.66
OtherMedia	0.55
Oxygen	100
Vitamins	0.26

Total **200**

PRODUCTS

Components	Mass Coeff %
Biomass	34.26
Carb. Dioxide	69.41
DeadBiomass	3.51
MAB	7.03
Water	61.5
Lactate	24.29

200

Unit: P-3/BBS-101

Process Description:

Bag Bioreactor 1

A pre-sterilized disposable bioreactor chamber equipped with ports for sterile aeration, seeding, harvesting, sampling, and analysis.

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components	
				Theoretical	SuperPro
AAs	0.08843	AAs		0.08733	0.08625
Biomass	0.00189	Biomass		0.01393	0.01393
DeadBiomass	0.00019	DeadBiomass		0.00143	0.00143
Glucose	0.37423	Glucose		0.36412	0.36514
Glutamine	0.04329	Glutamine		0.04222	0.04222
Inorganic Salts	0.90654	Inorganic Salts		0.88421	0.88416
Lactate	0.00134	Lactate		0.00989	0.00988
MAB	0.00039	MAB		0.00288	0.00286
OtherMedia	0.00783	OtherMedia		0.00765	0.00764
Vitamins	0.0037	Vitamins		0.00361	0.00361
Water	0.00339	Water		0.02501	0.02501
WFI	70.04777	WFI		70.04782	70.04782
TOTAL (kg/batch)	71.47899			71.49213	71.48995

Reaction Extent: 80%

EQUATION

REACTANTS

Components	Mass Coeff %
AAs	6.21
Glucose	26.28
Glutamine	3.04
Inorganic Salts	63.66
OtherMedia	0.55
Oxygen	100
Vitamins	0.26

Total 200

PRODUCTS

Components	Mass Coeff %
Biomass	34.26
Carb. Dioxide	69.41
DeadBiomass	3.51
MAB	7.03
Water	61.5
Lactate	24.29

200

Unit: P-4/BBS-102

Process Description:

Bag Bioreactor 2

A pre-sterilized disposable bioreactor chamber equipped with ports for sterile aeration, seeding, harvesting, sampling, and analysis.

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components	
				Theoretical	SuperPro
AAs	0.39911	AAs		0.39415	0.38837
Biomass	0.01393	Biomass		0.07322	0.07321
DeadBiomass	0.00143	DeadBiomass		0.00741	0.00751
Glucose	1.68901	Glucose		1.65221	1.64354
Glutamine	0.19538	Glutamine		0.19012	0.19012
Inorganic Salts	4.0914	Inorganic Salts		3.98127	3.98127
Lactate	0.00988	Lactate		0.05192	0.05191
MAB	0.00286	MAB		0.01511	0.01502
OtherMedia	0.03535	OtherMedia		0.03444	0.03441
Vitamins	0.01671	Vitamins		0.01625	0.01626
Water	0.02501	Water		0.13141	0.13141
WFI	316.91374	WFI		316.9137	316.91414
TOTAL (kg/batch)	323.39381			323.4672331	323.44717

Reaction Extent: 80%

EQUATION

REACTANTS

Components	Mass Coeff %
AAs	6.21
Glucose	26.28
Glutamine	3.04
Inorganic Salts	63.66
OtherMedia	0.55
Oxygen	100
Vitamins	0.26

Total 200

PRODUCTS

Components	Mass Coeff %
Biomass	34.26
Carb. Dioxide	69.41
DeadBiomass	3.51
MAB	7.03
Water	61.5
Lactate	24.29

200

Unit: P-9/SBR-101

Seed Bioreactor 1

Process Description:

Bioreactor used for continued cell growth and production of monoclonal antibodies.

Main Components

Inlet Components (kg/batch)		Outlet Components (kg/batch)	Theoretical	SuperPro
AAs	1.75135	AAs	0.35023	0.35027
Biomass	0.07321	Biomass	7.81121	7.80284
DeadBiomass	0.00751	DeadBiomass	0.80002	0.79941
Glucose	7.41151	Glucose	1.49342	1.48231
Glutamine	0.85734	Glutamine	0.17122	0.17147
Inorganic Salts	17.95346	Inorganic Salts	3.59111	3.59069
Lactate	0.05191	Lactate	4.98001	5.53213
MAB	0.01502	MAB	1.61002	1.60111
OtherMedia	0.15511	OtherMedia	0.03112	0.03102
Vitamins	0.07333	Vitamins	0.01471	0.01467
Water	0.13141	Water	11.14202	14.00684
WFI	965.60863	WFI	965.60863	965.60863
TOTAL (kg/batch)	994.08977		997.60372	1000.99139

Reaction Extent: 80%

EQUATION

REACTANTS

Components	Mass Coeff %
AAs	6.21
Glucose	26.28
Glutamine	3.04
Inorganic Salts	63.66
OtherMedia	0.55
Oxygen	100
Vitamins	0.26

Total 200

PRODUCTS

Components	Mass Coeff %
Biomass	34.26
Carb. Dioxide	69.41
DeadBiomass	3.51
MAB	7.03
Water	61.5
Lactate	24.29

200

Unit: P-15/SBR-102

Seed Bioreactor 2

Process Description:

Bioreactor used for continued cell growth and production of monoclonal antibodies.

Main Components

Inlet Components (kg/batch)		Outlet Components (kg/batch)	Theoretical	SuperPro
AAs	4.52681	AAs	0.90521	0.90536
Biomass	7.80284	Biomass	22.81032	22.78205
DeadBiomass	0.79941	DeadBiomass	2.85423	2.84632
Glucose	19.15695	Glucose	3.82002	3.83139
Glutamine	2.21603	Glutamine	0.44402	0.44321
Inorganic Salts	46.40531	Inorganic Salts	9.28221	9.28106
Lactate	5.53213	Lactate	19.69731	19.69721
MAB	1.60111	MAB	5.71001	5.70075
OtherMedia	0.40092	OtherMedia	0.08019	0.08019
Vitamins	0.18953	Vitamins	0.03791	0.03791
Water	14.00684	Water	38.43123	39.87146
WFI	2976.90078	WFI	2976.90077	2976.90077
TOTAL (kg/batch)	3079.53866		3080.97343	3082.37768

Reaction Extent: 80%

EQUATION

REACTANTS

Components	Mass Coeff %
AAs	6.21
Glucose	26.28
Glutamine	3.04
Inorganic Salts	63.66
OtherMedia	0.55
Oxygen	100
Vitamins	0.26

Total 200

PRODUCTS

Components	Mass Coeff %
Biomass	34.26
Carb. Dioxide	69.41
DeadBiomass	3.51
MAB	7.03
Water	61.5
Lactate	24.29

200

Flexible Manufacturing Facility for Biopharmaceuticals

Unit: P-25/PBR-101

Production Bioreactor

Process Description:

Fed batch bioreactor used for continued cell growth and production of monoclonal antibodies at a 3.5 g/l titer.

Inlet Components (kg/batch)		Outlet Components (kg/batch)	Main Components	
			Theoretical	SuperPro
AAs	51.76737	AAs	3.44222	3.48472
Biomass	27.78205	Biomass	166.12232	167.26415
DeadBiomass	2.84632	DeadBiomass	16.98743	17.13652
Glucose	194.74019	Glucose	14.98641	14.74692
Glutamine	22.08257	Glutamine	1.65321	1.70588
Inorganic Salts	320.90032	Inorganic Salts	33.42423	35.72256
Lactate	19.69721	Lactate	118.58712	118.58862
MAB	5.70075	MAB	34.32111	34.32186
OtherMedia	2.54784	OtherMedia	0.30863	0.30863
Vitamins	1.20444	Vitamins	0.15231	0.14591
Water	39.87146	Water	300.04222	300.25526
WFI	9096.98831	WFI	9096.98831	9096.98831
TOTAL (kg/batch)	9786.12881		9787.00523	9790.66934

Reaction Extent: 80%

EQUATION

REACTANTS

Components	Mass Coeff %
AAs	6.21
Glucose	26.28
Glutamine	3.04
Inorganic Salts	63.66
OtherMedia	0.55
Oxygen	100
Vitamins	0.26

Total 200

PRODUCTS

Components	Mass Coeff %
Biomass	34.26
Carb. Dioxide	69.41
DeadBiomass	3.51
MAB	7.03
Water	61.5
Lactate	24.29

200

Unit: P-26/V-201

Blending Tank

Process Description:

Hold material from main bioreactor before transferring to centrifuge.

Inlet Components (kg/batch)		Outlet Components (kg/batch)	Main Components	
			Theoretical	SuperPro
AAs	3.49	AAs	3.49	3.49
Biomass	167.26	Biomass	167.26	167.26
DeadBiomass	17.14	DeadBiomass	17.14	17.14
Glucose	14.75	Glucose	14.75	14.75
Glutamine	1.71	Glutamine	1.71	1.71
Inorganic Salts	35.72	Inorganic Salts	35.72	35.72
Lactate	118.59	Lactate	118.59	118.59
MAB	34.32	MAB	34.32	34.32
OtherMedia	0.31	OtherMedia	0.31	0.31
Vitamins	0.15	Vitamins	0.15	0.15
Water	300.26	Water	300.26	300.26
WFI	9096.99	WFI	9096.99	9096.99
TOTAL (kg/batch)	9790.67		9790.67	9790.67

Unit: P-28/DS-201

Disk-Stack Centrifuge

Process Description:

Centrifuge to remove solids larger than 1 micron (98% of biomass removed).

Inlet Components (kg/batch)		Outlet Components (kg/batch)	Main Components		Waste Components	
			Theoretical	SuperPro	Theoretical	SuperPro
AAs	3.49	AAs	3.14	3.15	0.35	0.34
Biomass	167.26	Biomass	3.35	3.35	163.92	163.92
DeadBiomass	17.14	DeadBiomass	15.42	15.49	1.71	1.65
Glucose	14.75	Glucose	13.27	13.33	1.47	1.42
Glutamine	1.71	Glutamine	1.54	1.54	0.17	0.16
Inorganic Salts	35.72	Inorganic Salts	32.15	32.28	3.57	3.44
Lactate	118.59	Lactate	106.73	107.16	11.86	11.43
MAB	34.32	MAB	30.89	31.02	3.43	3.31
OtherMedia	0.31	OtherMedia	0.28	0.28	0.03	0.03
Vitamins	0.15	Vitamins	0.13	0.13	0.01	0.01
Water	300.26	Water	270.23	271.33	30.03	28.93
WFI	9096.99	WFI	8187.29	8220.53	909.70	876.46
TOTAL (kg/batch)	9790.67		8664.41	8699.58	1126.26	1091.09

Unit: P-30/DE-201

Process Description:

Sterile Filtration (Dead-end Filtration)

Removes bacteria and biomass.

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components		Waste Components	
				Theoretical	SuperPro	Theoretical	SuperPro
AAs	3.15	AAs		3.15	3.15	0.00	0.00
Biomass	3.35	Biomass		0.00	0.00	3.35	3.35
DeadBiomass	15.49	DeadBiomass		15.49	15.48	0.00	0.01
Glucose	13.33	Glucose		13.33	13.32	0.00	0.01
Glutamine	1.54	Glutamine		1.54	1.54	0.00	0.00
Inorganic Salts	32.28	Inorganic Salts		32.28	32.27	0.00	0.01
Lactate	107.16	Lactate		107.16	107.12	0.00	0.04
MAB	31.02	MAB		31.02	31.00	0.00	0.01
OtherMedia	0.28	OtherMedia		0.28	0.28	0.00	0.00
Vitamins	0.13	Vitamins		0.13	0.13	0.00	0.00
Water	271.33	Water		271.33	271.22	0.00	0.11
WFI	8220.53	WFI		8220.53	8217.36	0.00	3.18
TOTAL (kg/batch)	8699.58			8696.23	8692.87	3.35	6.71

Unit: P-32/V-202

Process Description:

Centrifugation

Hold outlet of centrifugation unit before entering cleavage bioreactor

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components	
				Theoretical	SuperPro
AAs	3.15	AAs		3.15	3.15
Biomass	0.00	Biomass		0.00	0.00
DeadBiomass	15.48	DeadBiomass		15.48	15.48
Glucose	13.32	Glucose		13.32	13.32
Glutamine	1.54	Glutamine		1.54	1.54
Inorganic Salts	32.27	Inorganic Salts		32.27	32.27
Lactate	107.12	Lactate		107.12	107.12
MAB	31.00	MAB		31.00	31.00
Nitrogen	0.00	Nitrogen		0.00	0.00
OtherMedia	0.28	OtherMedia		0.28	0.28
Oxygen	0.00	Oxygen		0.00	0.00
Vitamins	0.13	Vitamins		0.13	0.13
Water	271.22	Water		271.22	271.22
WFI	8217.36	WFI		8217.36	8217.36
TOTAL (kg/batch)	8692.87			8692.87	8692.87

Unit: P-34/UF-201

Process Description:

Ultrafiltration (*Papain Process)

Concentrate feed stream with a feed:retentate concentration of 17.5

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components		Waste Components	
				Theoretical	SuperPro	Theoretical	SuperPro
AAs	3.15	AAs		0.54	0.55	2.60	2.60
Cysteine-HCl	0.00	Cysteine-HCl		0.00	0.00	0.00	0.00
DeadBiomass	15.48	DeadBiomass		2.67	2.71	12.81	12.77
EDTA	0.00	EDTA		0.00	0.00	0.00	0.00
Glucose	13.32	Glucose		2.30	2.33	11.02	10.99
Glutamine	1.54	Glutamine		0.27	0.27	1.28	1.27
Inorganic Salts	32.27	Inorganic Salts		5.57	5.65	26.70	26.62
Lactate	107.12	Lactate		18.48	18.74	88.64	88.38
MAB	31.00	MAB		31.00	31.00	0.00	0.00
OtherMedia	0.28	OtherMedia		0.05	0.05	0.23	0.23
Sodium Phosphat	0.00	Sodium Phosphat		0.00	0.00	0.00	0.00
Vitamins	0.13	Vitamins		0.02	0.02	0.11	0.11
Water	271.22	Water		47.46	47.46	223.76	223.76
WFI	8217.36	WFI		1438.04	1437.88	6779.32	6779.48
TOTAL (kg/batch)	8692.87			1546.40	1546.66	7146.47	7146.21

Flexible Manufacturing Facility for Biopharmaceuticals

Unit: P-37/R-201

Stirred Reactor

Process Description:

Cleave the monoclonal antibody to 2 Fab' (or Fab) fragments and 1 Fc fragment with 95% efficiency, removing 60% of WFI.

Inlet Components (kg/batch)				Outlet		Main Components		Waste Components	
Stream name:	S-210	Dig Buf	Papain	Total		Theoretical	SuperPro	Theoretical	SuperPro
AAs		0.55	0.00	0.00	0.55	0.55	0.55	0.00	0.00
Cysteine-HCl		0.00	5.45	0.00	5.45	5.45	5.45	0.00	0.00
DeadBiomass		2.71	0.00	0.00	2.71	2.71	2.71	0.00	0.00
EDTA Disodium		0.00	9.02	0.00	9.02	9.02	9.02	0.00	0.00
Glucose		2.33	0.00	0.00	2.33	2.33	2.33	0.00	0.00
Glutamine		0.27	0.00	0.00	0.27	0.27	0.27	0.00	0.00
Inorganic Salts		5.65	0.00	0.00	5.65	5.65	5.65	0.00	0.00
Lactate		18.74	0.00	0.00	18.74	18.74	18.74	0.00	0.00
MAB		31.00	0.00	0.00	31.00	1.55	1.55	0.00	0.00
MAB Fab		0.00	0.00	0.00	0.00	58.91	58.91	0.00	0.00
Mab Fc		0.00	0.00	0.00	0.00	29.45	29.45	0.00	0.00
OtherMedia		0.05	0.00	0.00	0.05	0.05	0.05	0.00	0.00
Papain		0.00	0.00	1540.43	1540.43	1481.52	1481.52	0.00	0.00
Sodium Phosphat		0.00	4.20	0.00	4.20	4.20	4.20	0.00	0.00
Vitamins		0.02	0.00	0.00	0.02	0.02	0.02	0.00	0.00
Water		47.46	0.00	0.00	47.46	47.46	47.46	0.00	0.00
WFI		1437.88	1537.23	1540.43	4515.53	1806.21	1806.21	2709.32	2709.32
TOTAL (kg/batch)		1546.66	1555.90	3080.85	6183.41	3474.09	3474.09	2709.32	2709.32

Unit: P-39/PFF-201

Plate and Frame Filter

Process Description:

Removes unreacted Papain from the process stream.

Inlet Components (kg/batch)				Outlet		Main Components		Waste Components	
Stream name:	S-211	Tris-HCl	Total			Theoretical	SuperPro	Theoretical	SuperPro
AAs		0.55	0.00	0.55		0.51	0.51	0.04	0.04
Cysteine-HCl		5.45	0.00	5.45		5.06	5.03	0.38	0.41
DeadBiomass		2.71	0.00	2.71		2.52	2.50	0.19	0.21
EDTA Disodium		9.02	0.00	9.02		8.39	8.34	0.63	0.68
Glucose		2.33	0.00	2.33		2.16	2.15	0.17	0.18
Glutamine		0.27	0.00	0.27		0.25	0.25	0.02	0.02
Inorganic Salts		5.65	0.00	5.65		5.22	5.22	0.42	0.43
Lactate		18.74	0.00	18.74		17.34	17.33	1.41	1.42
MAB		1.55	0.00	1.55		1.44	1.43	0.11	0.12
MAB Fab		19.64	0.00	19.64		18.16	18.15	1.47	1.49
Mab Fc		9.82	0.00	9.82		9.08	9.07	0.74	0.74
OtherMedia		0.05	0.00	0.05		0.05	0.05	0.00	0.00
Papain		1540.43	0.00	1540.43		0.00	0.00	1540.43	1540.43
Sodium Phosphat		4.20	0.00	4.20		3.91	3.88	0.29	0.32
Tris HCl		0.00	206.78	206.78		160.25	160.92	46.53	45.86
Vitamins		0.02	0.00	0.02		0.02	0.02	0.00	0.00
Water		47.46	0.00	47.46		43.90	43.87	3.56	3.59
WFI		1806.21	2340.66	4146.88		3524.84	3491.04	622.03	655.84
TOTAL (kg/batch)		3474.09	2547.44	6021.53		3803.11	3769.77	2218.42	2251.77

Unit: P-42/DF-202

Diafiltration System

Process Description:

F(ab')₂ must be dissolved in Reduction Reaction Buffer at 10 mg/mL before Reduction (Concentrate from 3.68 mg/ml).

Inlet Components (kg/batch)			Outlet Components (kg/batch)		Main Components		Waste Components	
Stream name:	S-214	RR Buffer 2-1			Theoretical	SuperPro	Theoretical	SuperPro
AAs		0.13	0.00	AAs	0.02	0.01	0.11	0.62
DeadBiomass		0.65	0.00	DeadBiomass	0.10	0.03	0.00	0.00
EDTA, Sodium		0.00	1134.87	EDTA, Sodium	170.23	178.18	964.64	956.69
F(ab') ₂		16.67	0.00	F(ab') ₂	16.67	16.67	16.67	0.53
Glucose		0.56	0.00	Glucose	0.08	0.03	0.47	0.06
Glutamine		0.07	0.00	Glutamine	0.01	0.00	0.06	0.22
Impurities		0.44	0.00	Impurities	0.07	0.27	0.38	1.29
Inorganic Salts		1.35	0.00	Inorganic Salts	0.20	0.07	1.15	4.26
Lactate		4.48	0.00	Lactate	0.67	0.22	3.81	1.21
MAB		1.32	0.00	MAB	0.20	0.06	1.12	7.93
Mab Fc		8.34	0.00	MAB Fab	0.00	0.00	0.00	0.00
Nitrogen		0.00	0.00	Mab Fc	1.25	0.41	7.09	0.01
OtherMedia		0.01	0.00	OtherMedia	0.00	0.00	0.00	0.00
Oxygen		0.00	0.00	Oxygen	0.00	0.00	0.00	0.00
Sodium Acetate		6.27	0.00	Sodium Acetate	0.94	0.31	5.33	5.96
Sodium Phosphat		0.00	14477.03	Sodium Phosphat	2171.55	2272.91	12305.47	12204.11
TRIS HCl		147.46	0.00	TRIS HCl	22.12	7.28	125.34	140.17
Vitamins		0.01	0.00	Vitamins	0.00	0.00	0.01	0.01
Water		11.35	0.00	Water	1.70	0.56	9.65	10.79
WFI		3486.58	1524.37	WFI	522.99	411.49	2963.59	4599.46
TOTAL (kg/batch)		3685.68	17136.27	TOTAL (kg/batch)	2908.81	2888.50	16404.88	17933.44

Unit: P-44/R-202

Disulfide Reaction

Process Description:F(ab')₂ fragments are reacted with Reduction Agent 2-MEA to Form 2 Fab' Fragments.

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components	
				Theoretical	SuperPro
Stream name:	S-216	2-MEA			
2-MEA	0.00	8.00 2-MEA		8.00	8.00
AAs	0.01	0.00 AAs		0.01	0.01
DeadBiomass	0.03	0.00 DeadBiomass		0.03	0.03
EDTA, Sodium	178.18	0.00 EDTA, Sodium		178.18	178.18
F(ab') ₂	16.67	0.00 F(ab') ₂		0.00	0.00
Glucose	0.03	0.00 Glucose		0.03	0.03
Glutamine	0.00	0.00 Glutamine		0.00	0.00
Impurities	0.27	0.00 Impurities		0.27	0.27
Inorganic Salts	0.07	0.00 Inorganic Salts		0.07	0.07
Lactate	0.22	0.00 Lactate		0.22	0.22
MAB	0.06	0.00 MAB		0.06	0.06
MAB Fab	0.00	0.00 MAB Fab		15.84	16.67
Mab Fc	0.41	0.00 Mab Fc		0.41	0.41
OtherMedia	0.00	0.00 OtherMedia		0.00	0.00
Sodium Acetate	0.31	0.00 Sodium Acetate		0.31	0.31
Sodium Phosphat	2272.91	0.00 Sodium Phosphat		2272.91	2272.91
TRIS HCl	7.28	0.00 TRIS HCl		7.28	7.28
Vitamins	0.00	0.00 Vitamins		0.00	0.00
Water	0.56	0.00 Water		0.56	0.56
WFI	411.49	0.00 WFI		411.49	411.49
TOTAL (kg/batch)	2888.50	8.00 TOTAL (kg/batch)		2895.67	2896.50

Unit: P-47/DF-203

Diafiltration System

Process Description:

2-MEA must be filtered out and Fab' must be dissolved in WFI at 10 mg/mL before Protein-A Chromatography.

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components		Waste Components	
				Theoretical	SuperPro	Theoretical	SuperPro
Stream name:	S-218	WFI In 2-3					
2-MEA	8.00	0.00 2-MEA		1.20	1.08	6.80	6.92
AAs	0.01	0.00 AAs		0.00	0.00	0.01	0.01
DeadBiomass	0.03	0.00 DeadBiomass		0.00	0.00	0.03	0.03
EDTA, Sodium	178.18	0.00 EDTA, Sodium		26.73	24.11	151.45	154.06
Glucose	0.03	0.00 Glucose		0.00	0.00	0.02	0.02
Glutamine	0.00	0.00 Glutamine		0.00	0.00	0.00	0.00
Impurities	0.27	0.00 Impurities		0.04	0.18	0.23	0.09
Inorganic Salts	0.07	0.00 Inorganic Salts		0.01	0.01	0.06	0.06
Lactate	0.22	0.00 Lactate		0.03	0.03	0.19	0.19
MAB	0.06	0.00 MAB		0.01	0.01	0.05	0.05
MAB Fab	16.67	0.00 MAB Fab		16.67	16.67	0.00	0.00
Mab Fc	0.41	0.00 Mab Fc		0.06	0.06	0.35	0.36
Nitrogen	0.00	0.00 Nitrogen		0.00	0.00	0.00	0.00
OtherMedia	0.00	0.00 OtherMedia		0.00	0.00	0.00	0.00
Oxygen	0.00	0.00 Oxygen		0.00	0.00	0.00	0.00
Sodium Acetate	0.31	0.00 Sodium Acetate		0.05	0.04	0.26	0.27
Sodium Phosphat	2272.91	0.00 Sodium Phosphat		340.94	307.61	1931.97	1965.30
TRIS HCl	7.28	0.00 TRIS HCl		1.09	0.99	6.19	6.30
Vitamins	0.00	0.00 Vitamins		0.00	0.00	0.00	0.00
Water	0.56	0.00 Water		0.08	0.08	0.48	0.49
WFI	411.49	2868.63 WFI		492.02	1281.16	2788.10	1998.97
TOTAL (kg/batch)	2896.50	2868.63 TOTAL (kg/batch)		878.94	1632.02	4886.19	4133.11

Flexible Manufacturing Facility for Biopharmaceuticals

Unit: P-49/C-201 Protein-A Chromatography column
 Process Description: Remove the Fc fragments from the product stream.

Inlet Components (kg/batch)		Outlet Components (kg/batch)						Main Components		Waste Components	
								Theoretical	SuperPro	Theoretical	SuperPro
Stream name:	S-214	ProtA-Equil	ProtA-Wash	ProtA-Elut	ProtA-Reg	Total					
AAs	0.51	0.00		0.00	0.00	0.51		0.51	0.51	0.00	0.00
Acetic-Acid	0.00	0.00		0.00	15.80	0.00	15.80	6.32	6.32	9.48	9.48
Cysteine-HCl	5.03	0.00		0.00	0.00	0.00	5.03	5.03	5.03	0.00	0.00
DeadBiomass	2.50	0.00		0.00	0.00	0.00	2.50	2.50	2.50	0.00	0.00
EDTA Disodium	8.34	0.00		0.00	0.00	0.00	8.34	8.34	8.34	0.00	0.00
EDTA, Sodium	0.00	5.25		6.34	0.00	0.00	11.59	0.00	0.00	11.59	11.59
Glucose	2.15	0.00		0.00	0.00	0.00	2.15	2.15	2.15	0.00	0.00
Glutamine	0.25	0.00		0.00	0.00	0.00	0.25	0.25	0.25	0.00	0.00
Inorganic Salts	5.22	0.00		0.00	0.00	0.00	5.22	5.22	5.22	0.00	0.00
Lactate	17.33	0.00		0.00	0.00	0.00	17.33	17.33	17.33	0.00	0.00
MAB	1.43	0.00		0.00	0.00	0.00	1.43	0.00	0.00	1.43	1.43
MAB Fab	18.15	0.00		0.00	0.00	0.00	18.15	18.15	18.15	0.00	0.00
Mab Fc	9.07	0.00		0.00	0.00	0.00	9.07	0.00	0.00	9.07	9.07
OtherMedia	0.05	0.00		0.00	0.00	0.00	0.05	0.05	0.05	0.00	0.00
Sodium Chloride	0.00	0.00		3.17	0.00	0.00	3.17	0.00	0.00	3.17	5.79
Sodium Citrate	0.00	2.62		0.00	0.00	2.85	5.47	0.00	0.00	5.47	2.85
Sodium Phosphat	3.88	0.00		0.00	0.00	0.00	3.88	3.88	3.88	0.00	0.00
TRIS Base	0.00	2.62		3.17	0.00	0.00	5.79	0.00	0.00	5.79	5.79
TRIS HCl	160.92	7.87		9.51	0.00	0.00	178.30	160.47	160.92	17.83	17.38
Vitamins	0.02	0.00		0.00	0.00	0.00	0.02	0.02	0.02	0.00	0.00
Water	43.87	0.00		0.00	0.00	0.00	43.87	43.87	43.87	0.00	0.00
WFI	3491.04	2604.09		3148.88	2618.08	1578.25	13440.33	4475.63	4538.27	8964.70	8902.06
TOTAL (kg/batch)	3769.77	2622.45		3171.08	2633.88	1581.09	13778.26	4749.72	4812.81	9028.54	8965.45

Unit: P-51/DE-202 Sterile Filtration (Dead-end Filtration)
 Process Description: Removes bacteria and biomass.

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components		Waste Components	
				Theoretical	SuperPro	Theoretical	SuperPro
AAs	0.51	AAs		0.51	0.51	0.00	0.00
Acetic-Acid	6.32	Acetic-Acid		6.32	6.32	0.00	0.00
Cysteine-HCl	5.03	Cysteine-HCl		5.03	5.03	0.00	0.00
DeadBiomass	2.50	DeadBiomass		0.00	0.00	2.50	2.50
EDTA Disodium	8.34	EDTA Disodium		8.34	8.34	0.00	0.00
Glucose	2.15	Glucose		2.15	2.15	0.00	0.00
Glutamine	0.25	Glutamine		0.25	0.25	0.00	0.00
Impurities	0.00	Impurities		0.00	0.00	0.00	0.00
Inorganic Salts	5.22	Inorganic Salts		5.22	5.22	0.00	0.00
Lactate	17.33	Lactate		17.32	17.32	0.01	0.01
MAB Fab	18.15	MAB Fab		18.14	18.14	0.01	0.01
OtherMedia	0.05	OtherMedia		0.05	0.05	0.00	0.00
Oxygen	0.00	Oxygen		0.00	0.00	0.00	0.00
Sodium Phosphat	3.88	Sodium Phosphat		3.88	3.88	0.00	0.00
TRIS HCl	160.92	TRIS HCl		160.84	160.84	0.08	0.08
Vitamins	0.02	Vitamins		0.02	0.02	0.00	0.00
Water	43.87	Water		43.84	43.84	0.02	0.02
WFI	4538.27	WFI		4536.00	4535.98	2.27	2.29
TOTAL (kg/batch)	4812.81	TOTAL (kg/batch)		4812.81	4807.88	4.89	4.93

Unit: P-54/DF-204 Diafiltration
 Process Description: Further refine the product by exchanging buffer.

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components		Waste Components	
				Theoretical	SuperPro	Theoretical	SuperPro
Stream Name:	S-218	WFI-input	Total				
AAs	0.51	0.00	0.51	0.01	0.01	0.50	0.50
Acetic-Acid	6.32	0.00	6.32	0.16	0.17	6.16	6.15
Cysteine-HCl	5.03	0.00	5.03	0.13	0.13	4.91	4.90
DeadBiomass	0.00	0.00	0.00	0.00	0.00	0.00	0.00
EDTA Disodium	8.34	0.00	8.34	0.21	0.22	8.13	8.12
Glucose	2.15	0.00	2.15	0.05	0.06	2.10	2.10
Glutamine	0.25	0.00	0.25	0.01	0.01	0.24	0.24
Inorganic Salts	0.00	0.00	0.00	0.00	0.26	0.00	0.28
Lactate	5.22	0.00	5.22	0.13	0.14	5.09	5.08
MAB Fab	17.32	0.00	17.32	0.43	0.46	16.88	16.86
Nitrogen	18.14	0.00	18.14	18.14	17.60	0.00	0.00
OtherMedia	0.05	0.00	0.05	0.00	0.00	0.04	0.04
Oxygen	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Sodium Phosphat	3.88	0.00	3.88	0.10	0.10	3.78	3.78
TRIS HCl	160.84	0.00	160.84	4.02	4.29	156.82	156.55
Vitamins	0.02	0.00	0.02	0.00	0.00	0.02	0.02
Water	43.84	0.00	43.84	1.10	1.17	42.75	42.68
WFI	4535.98	1894.89	6430.87	932.48	924.60	5498.39	5506.27
TOTAL (kg/batch)	4807.88	1894.89	6702.77	956.96	949.22	5745.81	5753.55

Unit: P-56/V-207

Chemical Virus Inactivation Tank

Process Description:

Inactivate possible viruses through treatment with polysorbate 80.

				Main Components	
Inlet Components (kg/batch)		Outlet Components (kg/batch)		Theoretical	SuperPro
Stream Name:	S-222	Polysorb80	Total		
AAs		0.01	0.00	0.01	0.01
Acetic-Acid		0.17	0.00	0.17	0.17
Cysteine-HCl		0.13	0.00	0.13	0.13
DeadBiomass		0.00	0.00	0.00	0.00
EDTA Disodium		0.22	0.00	0.22	0.22
Glucose		0.06	0.00	0.06	0.06
Glutamine		0.01	0.00	0.01	0.01
Impurities		0.26	0.00	0.26	0.26
Inorganic Salts		0.14	0.00	0.14	0.14
Lactate		0.46	0.00	0.46	0.46
MAB Fab		17.60	0.00	17.60	17.60
OtherMedia		0.00	0.00	0.00	0.10
Polysorbate 80		0.00	0.10	0.10	0.00
Sodium Phosphat		0.10	0.00	0.10	0.10
TRIS HCl		4.29	0.00	4.29	4.29
Vitamins		0.00	0.00	0.00	0.00
Water		1.17	0.00	1.17	1.17
WFI		924.60	0.10	924.69	924.69
TOTAL (kg/batch)		949.22	0.19	949.41	949.41

Unit: P-58/DE-203

Sterile Filtration (Dead-end Filtration)

Process Description:

Further refines the stream.

				Main Components	
Inlet Components (kg/batch)		Outlet Components (kg/batch)		Theoretical	SuperPro
AAs	0.01	AAs		0.01	0.01
Acetic-Acid	0.17	Acetic-Acid		0.17	0.17
Cysteine-HCl	0.13	Cysteine-HCl		0.13	0.13
EDTA Disodium	0.22	EDTA Disodium		0.22	0.22
Glucose	0.06	Glucose		0.06	0.06
Glutamine	0.01	Glutamine		0.01	0.01
Impurities	0.26	Impurities		0.26	0.26
Inorganic Salts	0.14	Inorganic Salts		0.14	0.14
Lactate	0.46	Lactate		0.46	0.46
MAB Fab	17.60	MAB Fab		17.60	17.60
Nitrogen	0.00	Nitrogen		0.00	0.00
OtherMedia	0.00	OtherMedia		0.00	0.00
Oxygen	0.00	Oxygen		0.00	0.00
Polysorbate 80	0.10	Polysorbate 80		0.10	0.10
Sodium Phosphat	0.10	Sodium Phosphat		0.10	0.10
TRIS HCl	4.29	TRIS HCl		4.29	4.29
Vitamins	0.00	Vitamins		0.00	0.00
Water	1.17	Water		1.17	1.17
WFI	924.69	WFI		924.69	924.69
TOTAL (kg/batch)	949.41	TOTAL (kg/batch)		949.41	949.41

Flexible Manufacturing Facility for Biopharmaceuticals

Unit: P-68/C-301 Cation Exchange Chromatography
 Process Description: Binds Fab fragments, allowing impurities to flow through (95% binding, 95% yield).

Inlet Components (kg/batch)		Main Components							Waste Components	
		Outlet Components (kg/batch)							Theoretical	SuperPro
Stream name:	Fab Load	Cat-Equil	Cat Wash	Cat Elute	Cat-WFI	Cat-Strip	Total			
2-MEA	0.02794	0.00		0.00	0.00	0.00	0.03		0.00	0.00
AAs	0.00002	0.00		0.00	0.00	0.00	0.00		0.00	0.00
Acetic-Acid	0.00132	0.00		0.00	0.00	0.00	0.00		0.00	0.00
EDTA, Sodium	0.62195	0.00		0.00	0.00	0.00	0.62		0.00	0.62
Glucose	0.0001	0.00		0.00	0.00	0.00	0.00		0.00	0.00
Glutamine	0.00001	0.00		0.00	0.00	0.00	0.00		0.00	0.00
Impurities	0.06612	0.00		0.00	0.00	0.00	0.07		0.01	0.00793
Inorganic Salts	0.00023	0.00		0.00	0.00	0.00	0.00		0.00	0.00
Lactate	0.00077	0.00		0.00	0.00	0.00	0.00		0.00	0.00
MAB Fab	16.67308	0		0	0	0	16.67		15.05	15.04746
MES	25.47882	5.30362		5.30362	3.99882	0.00	5.09965		0.53	0.53318
OtherMedia	0	0.00		0.00	0.00	0.00	0.00		0.00	0.00
Polysorbate 80	0.02949	0.00		0.00	0	0.00	0		0.00	0
Sodium Acetate	0.00108	0.00		0.00	0	0	0.00		0.00	0
Sodium Chloride	0	0.00		0.00	23.94348	0	30.53481		3.19	3.19246
Sodium Phosphat	7.93396	0.00		0.00	0.00	0.00	7.93		0.00	0.00
TRIS HCl	0.02542	0.00		0.00	0.00	0.00	0.03		0.00	0.00
Vitamins	0	0.00		0.00	0.00	0.00	0.00		0.00	0.00
Water	0.00196	0.00		0.00	0.00	0.00	0.00		0.00	0.00
WFI	2853.99631	537.98904		537.98904	409.70927	1203.86659	1718.88173		215.14	215.14345
TOTAL (kg/batch)	2904.86	543.29		543.29	437.65	1203.87	1723.98		233.90	233.92

Unit: P-71/C-302 Anion Exchange Chromatography
 Process Description: Binds Impurities, allowing FAB to flow through (5% binding, 95% yield of FAB).

Inlet Components (kg/batch)		Main Components							Waste Components	
		Outlet Components (kg/batch)							Theoretical	SuperPro
Stream name:	S-304 (Load)	Anion-Equil	Anion-Wash	Anion-Strip	Total					
Impurities	0.00793	0		0	0.00793		0.00	0.0004	0.01	0.00754
MAB Fab	15.04746	0		0	15.04746		15.01	15.00984	0.04	0.03762
MES	0.53318	0		0	0.53318		0.53	0.53318	0.00	0
Sodium Chloride	11.92664	0.72322		0.28929	26.11021		12.22	12.21593	26.83	26.83343
TRIS Base	14.76077	1.22224		0.4889	2.23362		15.25	15.24966	3.46	3.45586
WFI	3685.32078	287.3425		114.937	446.79333		3800.26	3800.25778	734.14	734.13582
Total (kg/batch)	3727.59676	289.28796		115.71519	475.13716		3843.26	3843.26679	764.5	764.47027

Unit: P-81/DF-401 Diafiltration System
 Process Description: Fab' must be dissolved in Reduction Reaction Buffer at 10 mg/mL before Reduction (Concentrate from 6 mg/ml).

Inlet Components (kg/batch)		Main Components							Waste Components	
		Outlet Components (kg/batch)							Theoretical	SuperPro
Stream Name:	S-401	RR Buffer								
EDTA, Sodium		0.00	5.69	EDTA, Sodium		0.85	0.94	4.84	4.75	
Impurities		0.00	0.00	Impurities		0.00	0.00	0.00	0.00	
MAB Fab		15.01	0.00	MAB Fab		15.01	15.01	0.00	0.00	
MES		0.53	0.00	MES		0.08	0.03	0.45	0.51	
Nitrogen		0.00	0.00	Phosphate		10.89	11.95	61.71	60.65	
Oxygen		0.00	0.00	Reduced Mab Fab		0.00	0.00	0.00	0.00	
Phosphate		0.00	72.60	Sodium Chloride		1.83	0.63	10.38	11.58	
Sodium Chloride		12.22	0.00	TRIS Base		2.29	0.79	12.96	14.46	
TRIS Base		15.25	0.00	WFI		1716.72	1454.82	9728.09	9989.99	
WFI		3800.26	7644.56	TOTAL (kg/batch)		1747.68	1484.17	9818.44	10081.95	
TOTAL (kg/batch)		3843.27	7722.85							

Unit: P-83 / R-401 Thiol Reduction Reaction
 Process Description: Remove any small-thiol reactive molecules which can cap cysteine during purification steps.

Inlet Components (kg/batch)		Main Components							Waste Components	
		Outlet Components (kg/batch)							Theoretical	SuperPro
Stream Name:	S-403	2-MEA								
2-MEA		0.00	9.01	2-MEA		9.01	9.01	9.01	9.01	
EDTA, Sodium		0.94	0.00	EDTA Disodium		0.00	0.00	0.00	0.00	
Impurities		0.00	0.00	EDTA, Sodium		0.94	0.94	0.94	0.94	
MAB Fab		15.01	0.00	Impurities		0.00	0.00	0.00	0.00	
MES		0.03	0.00	MAB Fab		0.75	0.75	0.75	0.75	
Phosphate		11.95	0.00	MES		0.03	0.03	0.03	0.03	
Reduced Mab Fab		0.00	0.00	Phosphate		11.95	11.95	11.95	11.95	
Sodium Chloride		0.63	0.00	Reduced Mab Fab		14.26	14.26	14.26	14.26	
TRIS Base		0.79	0.00	Sodium Chloride		0.63	0.63	0.63	0.63	
WFI		1454.82	0.00	TRIS Base		0.79	0.79	0.79	0.79	
TOTAL (kg/batch)		1484.17	9.01	WFI		1454.82	1454.82	1454.82	1454.82	
				TOTAL (kg/batch)		1493.18	1493.17	1493.17	1493.17	

Flexible Manufacturing Facility for Biopharmaceuticals

Unit: P-86/DF-402

Diafiltration System

Process Description: Separate out 2-MEA and keep Fab' at 10 mg/mL in PEGylation Reaction Buffer.

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components		Waste Components	
				Theoretical	SuperPro	Theoretical	SuperPro
Stream Name:	S-405	PR Buffer 4-1					
2-MEA	9.01	0.00 2-MEA		1.35	1.22	7.66	7.79
EDTA Disodium	0.00	2.23 EDTA Disodium		0.33	0.95	1.89	1.27
EDTA, Sodium	0.94	0.00 EDTA, Sodium		0.14	0.13	0.14	0.81
Impurities	0.00	0.00 Impurities		0.00	0.00	0.00	0.00
MAB Fab	0.75	0.00 MAB Fab		0.75	0.75	0.00	0.00
MES	0.03	0.00 MES		0.00	0.00	0.02	0.02
Nitrogen	0.00	0.00 PEG		0.00	0.00	0.00	0.00
Oxygen	0.00	0.00 Phosphate		6.05	13.78	34.31	26.59
Phosphate	11.95	28.41 Reduced Mab Fab		14.26	14.26	0.00	0.00
Reduced Mab Fab	14.26	0.00 Sodium Chloride		0.09	0.09	0.54	0.55
Sodium Chloride	0.63	0.00 TRIS Base		0.12	0.11	0.67	0.68
TRIS Base	0.79	0.00 WFI		1111.65	1477.31	3334.94	2969.27
WFI	1454.82	2991.76 TOTAL (kg/batch)		1134.75	1508.59	3380.16	3006.98
TOTAL (kg/batch)	1493.17	3022.40					

Unit: P-88/R-402

PEGylation Reaction

Process Description: PEGylate Fab' fragments at thiol in hinge region cysteine.

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components		Waste Components	
				Theoretical	SuperPro	Theoretical	SuperPro
Stream Name:	S-407	PEG Reagent					
2-MEA	1.22	0.00 2-MEA		1.22	1.22	0.00	0.00
EDTA Disodium	0.95	0.00 EDTA Disodium		0.95	0.95	0.00	0.00
EDTA, Sodium	0.13	0.00 EDTA, Sodium		0.13	0.13	0.00	0.00
Impurities	0.00	0.00 Impurities		0.00	0.00	0.00	0.00
MAB Fab	0.75	0.00 MAB Fab		0.75	0.75	0.00	0.00
MES	0.00	0.00 MES		0.00	0.00	0.00	0.00
PEG	0.00	228.15 Nitrogen		0.00	0.00	0.00	0.00
Phosphate	13.78	0.00 Oxygen		0.00	0.00	0.00	0.00
Reduced Mab Fab	14.26	0.00 PEG		216.74	217.31	0.00	0.00
Sodium Chloride	0.09	0.00 PEGylated Mab F		27.09	24.38	0.00	0.00
TRIS Base	0.11	0.00 Phosphate		13.78	13.78	0.00	0.00
WFI	1477.31	0.00 Reduced Mab Fab		1.43	0.71	0.00	0.00
TOTAL (kg/batch)	1508.59	228.15 Sodium Chloride		0.09	0.09	0.00	0.00
		TRIS Base		0.11	0.11	0.00	0.00
		WFI		590.92	590.92	886.39	886.39
		TOTAL (kg/batch)		853.21	850.36	886.39	886.39

Unit: P-91/DF-403

Diafiltration System

Process Description: Filter out PEG Reagent and make sure pH between 3 and 12.

Inlet Components (kg/batch)		Outlet Components (kg/batch):		Main Components		Waste Components	
				Theoretical	SuperPro	Theoretical	SuperPro
Stream Name:	S-409	WFI In 4-4					
2-MEA	1.22	0.00 2-MEA		0.18	0.17	1.04	1.05
EDTA Disodium	0.95	0.00 EDTA Disodium		0.14	0.13	0.81	0.82
EDTA, Sodium	0.13	0.00 EDTA, Sodium		0.02	0.02	0.11	0.11
Impurities	0.00	0.00 Impurities		0.00	0.00	0.00	0.00
MAB Fab	0.75	0.00 MAB Fab		0.11	0.10	0.64	0.65
MES	0.00	0.00 MES		0.00	0.00	0.00	0.00
Nitrogen	0.00	0.00 PEG		32.60	29.41	184.72	187.90
Oxygen	0.00	0.00 PEGylated Mab F		24.38	24.38	0.00	0.00
PEG	217.31	0.00 Phosphate		2.07	1.87	11.71	11.91
PEGylated Mab F	24.38	0.00 Reduced Mab Fab		0.11	0.10	0.61	0.62
Phosphate	13.78	0.00 Sodium Chloride		0.01	0.01	0.07	0.07
Reduced Mab Fab	0.71	0.00 TRIS Base		0.02	0.01	0.09	0.09
Sodium Chloride	0.09	0.00 WFI		924.40	802.27	1386.60	1508.72
TRIS Base	0.11	0.00 TOTAL (kg/batch)		984.04	858.47	1586.39	1711.96
WFI	590.92	1720.07					
TOTAL (kg/batch)	850.36	1720.07					

Flexible Manufacturing Facility for Biopharmaceuticals

Unit: P-101 / C-401

Process Description:

Cation Exchange

Specifically binds PEGylated Fab' fragments which are larger and have lower surface charge.

Separates unPEGylated Fab' fragments and excess PEG molecules from Pegylated Fab'.

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components		Waste Components	
				Theoretical	SuperPro	Theoretical	SuperPro
Stream Name:	S-410						
2-MEA	0.17	2-MEA		0.00	0.00	0.17	0.17
EDTA Disodium	0.13	EDTA Disodium		0.00	0.00	0.13	0.13
EDTA, Sodium	0.02	EDTA, Sodium		0.00	0.00	0.02	0.02
Impurities	0.00	Impurities		0.00	0.00	0.00	0.00
MAB Fab	0.10	MAB Fab		0.00	0.00	0.10	0.10
MES	0.00	MacroCap SP		0.00	0.00	0.00	2026.87
PEG	29.41	MES		0.00	0.00	0.00	0.00
PEGylated Mab F	24.38	PEG		0.00	0.00	29.41	29.41
Phosphate	5.83	PEGylated Mab F		21.94	22.01	2.44	2.38
Reduced Mab Fab	0.10	Phosphate		0.87	0.28	4.95	11.94
Sodium Chloride	0.01	Reduced Mab Fab		0.00	0.00	0.10	0.10
TRIS Base	0.01	Sodium Chloride		0.00	8.50	0.01	98.78
Water	2084.92	TRIS Base		0.00	0.00	0.01	0.01
WFI	802.27	Water		0.00	0.00	2084.92	3618.45
TOTAL (kg/batch)	2947.35	WFI		320.91	302.65	481.36	3513.89
		TOTAL (kg/batch)		343.73	333.42	2603.62	9302.24

Unit: P-106/DE-501

Process Description:

RetroVirus Filtration

Removes Retrovirus (lets 99% of protein pass through, virus not modeled).

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components		Waste Components	
				Theoretical	SuperPro	Theoretical	SuperPro
Stream name:	S-503						
Impurities	0	Impurities		0.00	0	0.00	0
KCl	0.00034	KCl		0.00	0.00034	0.00	0
KH2PO4	0.00034	KH2PO4		0.00	0.00034	0.00	0
MAB Fab	0.00025	MAB Fab		0.00	0.00025	0.00	0
Na2HPO4	0.18921	Na2HPO4		0.19	0.189	0.00	0.0002
PEGylated Mab F	21.45594	PEGylated Mab F		21.24	21.24138	0.21	0.21456
Phosphate	0.02402	Phosphate		0.02	0.02399	0.00	0.00003
Sodium Chloride	2.11584	Sodium Chloride		2.11	2.11355	0.00	0.00229
WFI	196.84436	WFI		196.63	196.63112	0.21	0.21324
Total (kg/batch)	220.6303	Total (kg/batch)		220.20	220.19997	0.43	0.43032

Unit: P-107/DE-502

Process Description:

Parvovirus Filtration

Removes Retrovirus (lets 99% of protein pass through, virus not modeled).

Inlet Components (kg/batch)		Outlet Components (kg/batch)		Main Components		Waste Components	
				Theoretical	SuperPro	Theoretical	SuperPro
Stream name:	S-504						
Impurities	0	Impurities		0.00	0	0.00	0
KCl	0.00034	KCl		0.00	0.00034	0.00	0
KH2PO4	0.00034	KH2PO4		0.00	0.00034	0.00	0
MAB Fab	0.00025	MAB Fab		0.00	0.00025	0.00	0
Na2HPO4	0.189	Na2HPO4		0.19	0.1888	0.00	0.0002
PEGylated Mab F	21.24138	PEGylated Mab F		21.03	21.02897	0.21	0.21241
Phosphate	0.02399	Phosphate		0.02	0.02397	0.00	0.00003
Sodium Chloride	2.11355	Sodium Chloride		2.11	2.11128	0.00	0.00227
WFI	196.63112	WFI		196.42	196.42002	0.21	0.2111
Total (kg/batch)	220.19997	Total (kg/batch)		219.77	219.77397	0.43	0.42601

Appendix E – Material Safety Data Sheets

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Immobilized Pepsin	370
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PBS Phosphate Buffered Saline	402
Phosphoric acid, 85%	409
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POLYSORBATE 80	420
Sodium acetate anhydrous	426
Sodium bicarbonate	432
Sodium citrate dihydrate	438
Sodium hydroxide	444
Sodium Phosphate tribasic	451
Tris(hydroxymethyl)amino methane HCl	458
TRIS base	464

*MSDS for individual media components were left out for brevity and can be found on <http://www.sciencelab.com/msdsList.php>

Material Safety Data Sheet

Thermo
SCIENTIFIC

2-Mercaptoethylamine Hydrochloride

1. Product and company identification

Product name	: 2-Mercaptoethylamine Hydrochloride	
Synonym	: ethanethiol, 2-amino-, hydrochloride	
Chemical formula	: C2-H7-N-S.Cl-H	
Supplier	: Thermo Fisher Scientific Pierce Biotechnology P.O. Box 117 Rockford, IL 61105 United States 815.968.0747 or 800.874.3723	Manufacturer : Thermo Fisher Scientific Pierce Biotechnology P.O. Box 117 Rockford, IL 61105 United States 815.968.0747 800.874.3723
Product No.	: 0020408 1854450 1885690	
MSDS #	: 3756	
Validation date	: 5/23/2008.	
Print date	: 5/23/2008.	
Responsible name	: MSDS (Regulatory Affairs)	
<u>In case of emergency</u>	: CHEMTREC: Use of 800.424.9300 Substance/Preparation OUTSIDE US: 202.483.7616	: Refer to the instruction booklet for proper and intended use. Otherwise, contact supplier for specific applications.

2. Hazards identification

Physical state	: Solid. [Crystalline solid]
Odor	: Disagreeable and choking.
OSHA/HCS status	: This material is considered hazardous by the OSHA Hazard Communication Standard (29 CFR 1910.1200).
Emergency overview	: CAUTION ! MAY BE HARMFUL IF SWALLOWED. MAY CAUSE RESPIRATORY TRACT, EYE AND SKIN IRRITATION. CAN CAUSE TARGET ORGAN DAMAGE. Harmful if swallowed. Slightly irritating to the eyes, skin and respiratory system. Do not ingest. Avoid contact with eyes, skin and clothing. Can cause target organ damage. Use only with adequate ventilation. Keep container tightly closed and sealed until ready for use. Wash thoroughly after handling.
Routes of entry	: Eye contact. Inhalation. Ingestion.
<u>Potential acute health effects</u>	
Inhalation	: Slightly irritating to the respiratory system. Exposure to decomposition products may cause a health hazard. Serious effects may be delayed following exposure.
Ingestion	: Harmful if swallowed.
Skin	: Slightly irritating to the skin.
Eyes	: Slightly irritating to the eyes.
<u>Potential chronic health effects</u>	
Chronic effects	: Can cause target organ damage.
Carcinogenicity	: No known significant effects or critical hazards.
Mutagenicity	: No known significant effects or critical hazards.
Teratogenicity	: No known significant effects or critical hazards.
Developmental effects	: No known significant effects or critical hazards.
Fertility effects	: No known significant effects or critical hazards.

2. Hazards identification

Target organs : Causes damage to the following organs: gastrointestinal tract, skin.

Over-exposure signs/symptoms

Inhalation : Adverse symptoms may include the following:
respiratory tract irritation
coughing

Ingestion : No specific data.

Skin : Adverse symptoms may include the following:
irritation
redness

Eyes : Adverse symptoms may include the following:
irritation
watering
redness

Medical conditions aggravated by over-exposure : Pre-existing digestive disorders and disorders involving any other target organs mentioned in this MSDS as being at risk may be aggravated by over-exposure to this product.

The substance is not classified as dangerous according to Directive 67/548/EEC and its amendments.

Classification : Not classified.

See toxicological information (section 11)

3. Composition/information on ingredients

United States

<u>Name</u>	<u>CAS number</u>	<u>%</u>
2-Mercaptoethylamine Hydrochloride	156-57-0	98 - 100

Substance/preparation : Substance

There are no ingredients or additional ingredients present which, within the current knowledge of the supplier and in the concentrations applicable, are classified as hazardous to health or the environment and hence require reporting in this section.

4. First aid measures

Inhalation : Move exposed person to fresh air. Keep person warm and at rest. If not breathing, if breathing is irregular or if respiratory arrest occurs, provide artificial respiration or oxygen by trained personnel. It may be dangerous to the person providing aid to give mouth-to-mouth resuscitation. Get medical attention. If unconscious, place in recovery position and get medical attention immediately. Maintain an open airway. Loosen tight clothing such as a collar, tie, belt or waistband. In case of inhalation of decomposition products in a fire, symptoms may be delayed. The exposed person may need to be kept under medical surveillance for 48 hours.

Ingestion : Wash out mouth with water. Remove dentures if any. Move exposed person to fresh air. Keep person warm and at rest. If material has been swallowed and the exposed person is conscious, give small quantities of water to drink. Stop if the exposed person feels sick as vomiting may be dangerous. Do not induce vomiting unless directed to do so by medical personnel. If vomiting occurs, the head should be kept low so that vomit does not enter the lungs. Get medical attention. Never give anything by mouth to an unconscious person. If unconscious, place in recovery position and get medical attention immediately. Maintain an open airway. Loosen tight clothing such as a collar, tie, belt or waistband.

Skin contact : Flush contaminated skin with plenty of water. Remove contaminated clothing and shoes. Continue to rinse for at least 10 minutes. Get medical attention if symptoms occur. Wash clothing before reuse. Clean shoes thoroughly before reuse.

4 . First aid measures

- Eye contact** : Immediately flush eyes with plenty of water for at least 15 minutes, occasionally lifting the upper and lower eyelids. Check for and remove any contact lenses. Get medical attention if irritation occurs.
- Protection of first-aiders** : No action shall be taken involving any personal risk or without suitable training. It may be dangerous to the person providing aid to give mouth-to-mouth resuscitation.

See section 11 for more detailed information on health effects and symptoms.

5 . Fire-fighting measures

- Flammability of the product** : No specific fire or explosion hazard.
- Extinguishing media**
- Suitable** : Use an extinguishing agent suitable for the surrounding fire.
- Not suitable** : None known.
- Special exposure hazards** : Promptly isolate the scene by removing all persons from the vicinity of the incident if there is a fire. No action shall be taken involving any personal risk or without suitable training.
- Hazardous combustion products** : Decomposition products may include the following materials:
carbon oxides
nitrogen oxides
sulfur oxides
halogenated compounds
- Special protective equipment for fire-fighters** : Fire-fighters should wear appropriate protective equipment and self-contained breathing apparatus (SCBA) with a full face-piece operated in positive pressure mode.
- Special remarks on fire hazards** : Emits highly corrosive fumes when heated to decomposition. Emits very toxic fumes when heated to decomposition.

6 . Accidental release measures

- Personal precautions** : No action shall be taken involving any personal risk or without suitable training. Evacuate surrounding areas. Keep unnecessary and unprotected personnel from entering. Do not touch or walk through spilled material. Provide adequate ventilation. Wear appropriate respirator when ventilation is inadequate. Put on appropriate personal protective equipment (see section 8).
- Environmental precautions** : Avoid dispersal of spilled material and runoff and contact with soil, waterways, drains and sewers. Inform the relevant authorities if the product has caused environmental pollution (sewers, waterways, soil or air).
- Large spill** : Move containers from spill area. Approach release from upwind. Prevent entry into sewers, water courses, basements or confined areas. Vacuum or sweep up material and place in a designated, labeled waste container. Dispose of via a licensed waste disposal contractor. Note: see section 1 for emergency contact information and section 13 for waste disposal.
- Small spill** : Move containers from spill area. Vacuum or sweep up material and place in a designated, labeled waste container. Dispose of via a licensed waste disposal contractor.

7 . Handling and storage

- Handling** : Put on appropriate personal protective equipment (see section 8). Eating, drinking and smoking should be prohibited in areas where this material is handled, stored and processed. Workers should wash hands and face before eating, drinking and smoking. Do not ingest. Avoid contact with eyes, skin and clothing. Use only with adequate ventilation. Wear appropriate respirator when ventilation is inadequate. Keep in the original container or an approved alternative made from a compatible material, kept tightly closed when not in use. Empty containers retain product residue and can be hazardous. Do not reuse container.

7 . Handling and storage

- Storage** : Store between the following temperatures: 2 to 8°C (35.6 to 46.4°F). Store in accordance with local regulations. Store in original container protected from direct sunlight in a dry, cool and well-ventilated area, away from incompatible materials (see section 10) and food and drink. Keep container tightly closed and sealed until ready for use. Containers that have been opened must be carefully resealed and kept upright to prevent leakage. Do not store in unlabeled containers. Use appropriate containment to avoid environmental contamination.

8 . Exposure controls/personal protection

Europe

No exposure limit value known.

Consult local authorities for acceptable exposure limits.

- Recommended monitoring procedures** : If this product contains ingredients with exposure limits, personal, workplace atmosphere or biological monitoring may be required to determine the effectiveness of the ventilation or other control measures and/or the necessity to use respiratory protective equipment.

- Engineering measures** : Use only with adequate ventilation. If user operations generate dust, fumes, gas, vapor or mist, use process enclosures, local exhaust ventilation or other engineering controls to keep worker exposure to airborne contaminants below any recommended or statutory limits.

- Hygiene measures** : Wash hands, forearms and face thoroughly after handling chemical products, before eating, smoking and using the lavatory and at the end of the working period. Appropriate techniques should be used to remove potentially contaminated clothing. Wash contaminated clothing before reusing. Ensure that eyewash stations and safety showers are close to the workstation location.

Personal protection

- Respiratory** : Use a properly fitted, air-purifying or air-fed respirator complying with an approved standard if a risk assessment indicates this is necessary. Respirator selection must be based on known or anticipated exposure levels, the hazards of the product and the safe working limits of the selected respirator.
- Hands** : Chemical-resistant, impervious gloves complying with an approved standard should be worn at all times when handling chemical products if a risk assessment indicates this is necessary.
- Eyes** : Safety eyewear complying with an approved standard should be used when a risk assessment indicates this is necessary to avoid exposure to liquid splashes, mists, gases or dusts.
- Skin** : Personal protective equipment for the body should be selected based on the task being performed and the risks involved and should be approved by a specialist before handling this product.
- Environmental exposure controls** : Emissions from ventilation or work process equipment should be checked to ensure they comply with the requirements of environmental protection legislation. In some cases, fume scrubbers, filters or engineering modifications to the process equipment will be necessary to reduce emissions to acceptable levels.

9 . Physical and chemical properties

- Physical state** : Solid. [Crystalline solid]
- Color** : White.
- Odor** : Disagreeable and choking.
- Molecular weight** : 113.62 g/mole
- Molecular formula** : C2-H7-N-S.Cl-H
- pH** : 3.5 to 5 [Conc. (% w/w): 11.4%]
- Melting/freezing point** : 67 to 71°C (152.6 to 159.8°F)

9 . Physical and chemical properties

Solubility : Easily soluble in the following materials: cold water and hot water.

10 . Stability and reactivity

Chemical stability : The product is stable. Under normal conditions of storage and use, hazardous polymerization will not occur.

Conditions to avoid : No specific data.

Incompatible materials : No specific data.

Hazardous decomposition products : Under normal conditions of storage and use, hazardous decomposition products should not be produced.

Possibility of hazardous reactions : Will not occur.

11 . Toxicological information

United States

Acute toxicity

Product/ingredient name	Result	Species	Dose	Exposure
ethanethiol, 2-amino-, hydrochloride	TDLo Oral	Rat	800 mg/kg	-

Conclusion/Summary : Not available.

Chronic toxicity

Conclusion/Summary : Not available.

Carcinogenicity

Conclusion/Summary : Laboratory experiments have shown mutagenic effects. Can cause gastrointestinal disturbances.

Classification

Product/ingredient name	ACGIH	IARC	EPA	NIOSH	NTP	OSHA
ethanethiol, 2-amino-, hydrochloride	-	-	-	None.	-	None.

Mutagenicity

Conclusion/Summary : Not available.

Teratogenicity

Conclusion/Summary : Not available.

Reproductive toxicity

Conclusion/Summary : Not available.

Europe

Chronic effects : No known significant effects or critical hazards.

Carcinogenicity : No known significant effects or critical hazards.

Mutagenicity : No known significant effects or critical hazards.

Teratogenicity : No known significant effects or critical hazards.

Developmental effects : No known significant effects or critical hazards.

Fertility effects : No known significant effects or critical hazards.

12 . Ecological information

Environmental effects : No known significant effects or critical hazards.

United States

Aquatic ecotoxicity

Conclusion/Summary : Not available.

Other adverse effects : No known significant effects or critical hazards.

13 . Disposal considerations

Waste disposal : The generation of waste should be avoided or minimized wherever possible. Dispose of surplus and non-recyclable products via a licensed waste disposal contractor. Disposal of this product, solutions and any by-products should at all times comply with the requirements of environmental protection and waste disposal legislation and any regional local authority requirements. Avoid dispersal of spilled material and runoff and contact with soil, waterways, drains and sewers.

Hazardous waste : Within the present knowledge of the supplier, this product is not regarded as hazardous waste, as defined by EU Directive 91/689/EEC.

Disposal should be in accordance with applicable regional, national and local laws and regulations.

Refer to Section 7: HANDLING AND STORAGE and Section 8: EXPOSURE CONTROLS/PERSONAL PROTECTION for additional handling information and protection of employees.

14 . Transport information

Regulatory information	UN number	Proper shipping name	Classes	PG*
DOT Classification	UN3335	Aviation Regulated Solid, n.o.s. (2-Aminoethanethiol hydrochloride) (ethanethiol, 2-amino-, hydrochloride)	9	III
IATA-DGR Class	Not available.	Not available.	Not available.	-

PG* : Packing group

15 . Regulatory information

United States

HCS Classification : Target organ effects

U.S. Federal regulations : **United States inventory (TSCA 8b)**: This material is listed or exempted.

SARA 302/304/311/312 extremely hazardous substances: No products were found.

SARA 302/304 emergency planning and notification: No products were found.

SARA 302/304/311/312 hazardous chemicals: No products were found.

SARA 311/312 MSDS distribution - chemical inventory - hazard identification: No products were found.

Clean Water Act (CWA) 307: No products were found.

Clean Water Act (CWA) 311: No products were found.

Clean Air Act (CAA) 112 accidental release prevention: No products were found.

Clean Air Act (CAA) 112 regulated flammable substances: No products were found.

Clean Air Act (CAA) 112 regulated toxic substances: No products were found.

Canada

WHMIS (Canada) : Class D-2B: Material causing other toxic effects (Toxic).

15 . Regulatory information

Canadian lists : CEPA Toxic substances: This material is not listed.
 Canadian ARET: This material is not listed.
 Canadian NPRI: This material is not listed.
 Alberta Designated Substances: This material is not listed.
 Ontario Designated Substances: This material is not listed.
 Quebec Designated Substances: This material is not listed.

Canada inventory : Canada inventory: This material is listed or exempted.

EU regulations

Risk phrases : This product is not classified according to EU legislation.
 :

International regulations

International lists : Australia inventory (AICS): This material is listed or exempted.
 China inventory (IECSC): This material is listed or exempted.
 Korea inventory (KECI): This material is listed or exempted.
 Philippines inventory (PICCS): This material is listed or exempted.
 Japan inventory (ENCS): This material is listed or exempted.

16 . Other information

Label requirements : MAY BE HARMFUL IF SWALLOWED. MAY CAUSE RESPIRATORY TRACT, EYE AND SKIN IRRITATION. CAN CAUSE TARGET ORGAN DAMAGE.

Hazardous Material Information System (U.S.A.) :

Health	1
Flammability	0
Physical hazards	1

The customer is responsible for determining the PPE code for this material.

National Fire Protection Association (U.S.A.) :



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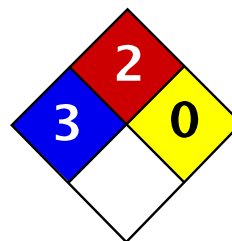
 Indicates information that has changed from previously issued version.

Notice to reader

To the best of our knowledge, the information contained herein is accurate. However, neither the above-named supplier, nor any of its subsidiaries, assumes any liability whatsoever for the accuracy or completeness of the information contained herein.

Final determination of suitability of any material is the sole responsibility of the user. All materials may present unknown hazards and should be used with caution. Although certain hazards are described herein, we cannot guarantee that these are the only hazards that exist.

This product has been classified according to the hazard criteria of the CPR and the MSDS contains all the information required by the CPR.



Health	3
Fire	2
Reactivity	0
Personal Protection	H

Material Safety Data Sheet

Acetic acid MSDS

Section 1: Chemical Product and Company Identification

Product Name: Acetic acid

Catalog Codes: SLA3784, SLA1438, SLA2101, SLA3604, SLA1258

CAS#: 64-19-7

RTECS: AF1225000

TSCA: TSCA 8(b) inventory: Acetic acid

CI#: Not applicable.

Synonym: Acetic acid; glacial acetic acid

Chemical Name: Acetic Acid, Glacial

Chemical Formula: C₂H₄O₂

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.
Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Acetic acid	64-19-7	100

Toxicological Data on Ingredients: Acetic acid: ORAL (LD50): Acute: 3310 mg/kg [Rat]. 4960 mg/kg [Mouse]. 3530 mg/kg [Rat]. DERMAL (LD50): Acute: 1060 mg/kg [Rabbit]. VAPOR (LC50): Acute: 5620 ppm 1 hours [Mouse].

Section 3: Hazards Identification

Potential Acute Health Effects:

Very hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation. Hazardous in case of skin contact (corrosive, permeator), of eye contact (corrosive). Liquid or spray mist may produce tissue damage particularly on mucous membranes of eyes, mouth and respiratory tract. Skin contact may produce burns. Inhalation of the spray mist may produce severe irritation of respiratory tract, characterized by coughing, choking, or shortness of breath. Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering.

Potential Chronic Health Effects:

Hazardous in case of skin contact (irritant), of ingestion, of inhalation.

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells. Mutagenic for bacteria and/or yeast.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

The substance may be toxic to kidneys, mucous membranes, skin, teeth.

Repeated or prolonged exposure to the substance can produce target organs damage. Repeated or prolonged contact with spray mist may produce chronic eye irritation and severe skin irritation. Repeated or prolonged exposure to spray mist may produce respiratory tract irritation leading to frequent attacks of bronchial infection.

Section 4: First Aid Measures

Eye Contact:

Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention immediately.

Skin Contact:

In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Cover the irritated skin with an emollient. Cold water may be used. Wash clothing before reuse. Thoroughly clean shoes before reuse. Get medical attention immediately.

Serious Skin Contact:

Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek immediate medical attention.

Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.

Serious Inhalation:

Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. If breathing is difficult, administer oxygen. If the victim is not breathing, perform mouth-to-mouth resuscitation. **WARNING:** It may be hazardous to the person providing aid to give mouth-to-mouth resuscitation when the inhaled material is toxic, infectious or corrosive. Seek immediate medical attention.

Ingestion:

Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. Loosen tight clothing such as a collar, tie, belt or waistband. Get medical attention if symptoms appear.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: Flammable.

Auto-Ignition Temperature: 463°C (865.4°F)

Flash Points: CLOSED CUP: 39°C (102.2°F). OPEN CUP: 43°C (109.4°F).

Flammable Limits: LOWER: 4% UPPER: 19.9%

Products of Combustion: These products are carbon oxides (CO, CO₂).

Fire Hazards in Presence of Various Substances:

Flammable in presence of open flames and sparks, of heat.

Slightly flammable to flammable in presence of oxidizing materials, of metals.

Explosion Hazards in Presence of Various Substances:

Risks of explosion of the product in presence of mechanical impact: Not available.

Risks of explosion of the product in presence of static discharge: Not available.

Slightly explosive in presence of oxidizing materials.

Fire Fighting Media and Instructions:

Flammable liquid, soluble or dispersed in water.

SMALL FIRE: Use DRY chemical powder.

LARGE FIRE: Use alcohol foam, water spray or fog. Cool containing vessels with water jet in order to prevent pressure build-up, autoignition or explosion.

Special Remarks on Fire Hazards:

Reacts with metals to produce flammable hydrogen gas.

It will ignite on contact with potassium-tert-butoxide.

A mixture of ammonium nitrate and acetic acid ignites when warmed, especially if warmed.

Special Remarks on Explosion Hazards:

Acetic acid vapors may form explosive mixtures with air.

Reactions between acetic acid and the following materials are potentially explosive: 5-azidotetrazole, bromine pentafluoride, chromium trioxide, hydrogen peroxide, potassium permanganate, sodium peroxide, and phosphorus trichloride.

Dilute acetic acid and dilute hydrogen can undergo an exothermic reaction if heated, forming peracetic acid which is explosive at 110 degrees C.

Reaction between chlorine trifluoride and acetic acid is very violent, sometimes explosive.

Section 6: Accidental Release Measures

Small Spill:

Dilute with water and mop up, or absorb with an inert dry material and place in an appropriate waste disposal container. If necessary: Neutralize the residue with a dilute solution of sodium carbonate.

Large Spill:

Flammable liquid. Corrosive liquid.

Keep away from heat. Keep away from sources of ignition. Stop leak if without risk. If the product is in its solid form: Use a shovel to put the material into a convenient waste disposal container. If the product is in its liquid form: Absorb with DRY earth, sand or other non-combustible material. Do not get water inside container.

Absorb with an inert material and put the spilled material in an appropriate waste disposal. Do not touch spilled material. Use water spray curtain to divert vapor drift. Prevent entry into sewers, basements or confined areas; dike if needed. Call for assistance on disposal. Neutralize the residue with a dilute solution of sodium carbonate. Be careful that the product is not present at a concentration level above TLV. Check TLV on the MSDS and with local authorities.

Section 7: Handling and Storage

Precautions:

Keep away from heat. Keep away from sources of ignition. Ground all equipment containing material. Do not ingest. Do not breathe gas/fumes/ vapor/spray. Never add water to this product. In case of insufficient ventilation, wear suitable respiratory equipment. If ingested, seek medical advice immediately and show the container or the label. Avoid contact with skin and eyes. Keep away from incompatibles such as oxidizing agents, reducing agents, metals, acids, alkalis.

Storage:

Store in a segregated and approved area. Keep container in a cool, well-ventilated area. Keep container tightly closed and sealed until ready for use. Avoid all possible sources of ignition (spark or flame).

Section 8: Exposure Controls/Personal Protection

Engineering Controls:

Provide exhaust ventilation or other engineering controls to keep the airborne concentrations of vapors below their respective threshold limit value. Ensure that eyewash stations and safety showers are proximal to the work-station location.

Personal Protection:

Splash goggles. Synthetic apron. Vapor respirator. Be sure to use an approved/certified respirator or equivalent.

Gloves (impervious).

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Vapor respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits:

TWA: 10 STEL: 15 (ppm) [Australia]

TWA: 25 STEL: 27 (mg/m³) [Australia]

TWA: 10 STEL: 15 (ppm) from NIOSH

TWA: 25 STEL: 37 (mg/m³) from NIOSH

TWA: 10 STEL: 15 (ppm) [Canada]

TWA: 26 STEL: 39 (mg/m³) [Canada]

TWA: 25 STEL: 37 (mg/m³)

TWA: 10 STEL: 15 (ppm) from ACGIH (TLV) [United States] [1999]

TWA: 10 (ppm) from OSHA (PEL) [United States]

TWA: 25 (mg/m³) from OSHA (PEL) [United States] Consult local authorities for acceptable exposure limits.

Section 9: Physical and Chemical Properties

Physical state and appearance: Liquid.

Odor: Pungent, vinegar-like, sour (Strong.)

Taste: Vinegar, sour (Strong.)

Molecular Weight: 60.05 g/mole

Color: Colorless. Clear (Light.)

pH (1% soln/water): 2 [Acidic.]

Boiling Point: 118.1°C (244.6°F)

Melting Point: 16.6°C (61.9°F)

Critical Temperature: 321.67°C (611°F)

Specific Gravity: 1.049 (Water = 1)

Vapor Pressure: 1.5 kPa (@ 20°C)

Vapor Density: 2.07 (Air = 1)

Volatility: Not available.

Odor Threshold: 0.48 ppm

Water/Oil Dist. Coeff.: The product is more soluble in water; log(oil/water) = -0.2

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water, diethyl ether, acetone.

Solubility:

Easily soluble in cold water, hot water.

Soluble in diethyl ether, acetone.

Miscible with Glycerol, alcohol, Benzene, Carbon Tetrachloride.

Practically insoluble in Carbon Disulfide.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Heat, ignition sources, incompatible materials

Incompatibility with various substances: Reactive with oxidizing agents, reducing agents, metals, acids, alkalis.

Corrosivity:

Highly corrosive in presence of stainless steel(304).

Slightly corrosive in presence of aluminum, of copper.

Non-corrosive in presence of stainless steel(316).

Special Remarks on Reactivity:

Reacts violently with strong oxidizing agents, acetaldehyde, and acetic anhydride. Material can react with metals, strong bases, amines, carbonates, hydroxides, phosphates, many oxides, cyanides, sulfides, chromic acid, nitric acid, hydrogen peroxide, carbonates, ammonium nitrate, ammonium thiosulfate, chlorine trifluoride, chlorosulfonic acid, perchloric acid, permanganates, xylene, oleum, potassium hydroxide, sodium hydroxide, phosphorus isocyanate, ethylenediamine, ethylene imine.

Special Remarks on Corrosivity: Moderate corrosive effect on bronze. No corrosion data on brass

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Absorbed through skin. Dermal contact. Eye contact. Inhalation. Ingestion.

Toxicity to Animals:

WARNING: THE LC50 VALUES HEREUNDER ARE ESTIMATED ON THE BASIS OF A 4-HOUR EXPOSURE.

Acute oral toxicity (LD50): 3310 mg/kg [Rat].

Acute dermal toxicity (LD50): 1060 mg/kg [Rabbit].

Acute toxicity of the vapor (LC50): 5620 1 hours [Mouse].

Chronic Effects on Humans:

MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells. Mutagenic for bacteria and/or yeast.

May cause damage to the following organs: kidneys, mucous membranes, skin, teeth.

Other Toxic Effects on Humans:

Extremely hazardous in case of inhalation (lung corrosive).

Very hazardous in case of skin contact (irritant), of ingestion, .

Hazardous in case of skin contact (corrosive, permeator), of eye contact (corrosive).

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: May affect genetic material and may cause reproductive effects based on animal data. No human data found.

Special Remarks on other Toxic Effects on Humans:

Acute Potential Health Effects:

Skin: Extremely irritating and corrosive. Causes skin irritation (reddening and itching, inflammation). May cause blistering, tissue damage and burns.

Eyes: Extremely irritating and corrosive. Causes eye irritation, lacrimation, redness, and pain. May cause burns, blurred vision, conjunctivitis, conjunctival and corneal destruction and permanent injury.

Inhalation: Causes severe respiratory tract irritation. Affects the sense organs (nose, ear, eye, taste), and blood. May cause chemical pneumonitis, bronchitis, and pulmonary edema. Severe exposure may result in lung tissue damage and corrosion (ulceration) of the mucous membranes. Inhalation may also cause rhinitis, sneezing, coughing, oppressive feeling in the chest or chest pain, dyspnea, wheezing, tachypnea, cyanosis, salivation, nausea, giddiness, muscular weakness.

Ingestion: Moderately toxic. Corrosive. Causes gastrointestinal tract irritation (burning and pain of the mouth, throat, and abdomen, coughing, ulceration, bleeding, nausea, abdominal spasms, vomiting, hematemesis, diarrhea. May Also affect the liver (impaired liver function), behavior (convulsions, giddiness, muscular weakness), and the urinary system - kidneys (Hematuria, Albuminuria, Nephrosis, acute renal failure, acute tubular necrosis). May also cause dyspnea or asphyxia. May also lead to shock, coma and death.

Chronic Potential Health Effects:

Chronic exposure via ingestion may cause blackening or erosion of the teeth and jaw necrosis, pharyngitis, and gastritis. It may also behavior (similar to acute ingestion), and metabolism (weight loss).

Chronic exposure via inhalation may cause asthma and/or bronchitis with cough, phlegm, and/or shortness of breath . It may also affect the blood (decreased leukocyte count), and urinary system (kidneys).

Repeated or prolonged skin contact may cause thickening, blackening, and cracking of the skin.

Section 12: Ecological Information

Ecotoxicity:

Ecotoxicity in water (LC50): 423 mg/l 24 hours [Fish (Goldfish)]. 88 ppm 96 hours [Fish (fathead minnow)]. 75 ppm 96 hours [Fish (bluegill sunfish)]. >100 ppm 96 hours [Daphnia].

BOD5 and COD: BOD-5: 0.34-0.88 g oxygen/g

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are less toxic than the product itself.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification:

CLASS 3: Flammable liquid.

Class 8: Corrosive material

Identification: : Acetic Acid, Glacial UNNA: 2789 PG: II

Special Provisions for Transport: Not available.

Section 15: Other Regulatory Information

Federal and State Regulations:

New York release reporting list: Acetic acid

Rhode Island RTK hazardous substances: Acetic acid

Pennsylvania RTK: Acetic acid

Florida: Acetic acid

Minnesota: Acetic acid

Massachusetts RTK: Acetic acid

New Jersey: Acetic acid

California Director's List of Hazardous Substances (8 CCR 339): Acetic acid

TSCA 8(b) inventory: Acetic acid

CERCLA: Hazardous substances.: Acetic acid: 5000 lbs. (2268 kg)

Other Regulations:

OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

EINECS: This product is on the European Inventory of Existing Commercial Chemical Substances.

Other Classifications:**WHMIS (Canada):**

CLASS B-3: Combustible liquid with a flash point between 37.8°C (100°F) and 93.3°C (200°F).

CLASS E: Corrosive liquid.

DSCL (EEC):

R10- Flammable.

R35- Causes severe burns.

S23- Do not breathe gas/fumes/vapour/spray

[***]

S26- In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

S45- In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).

HMIS (U.S.A.):

Health Hazard: 3

Fire Hazard: 2

Reactivity: 0

Personal Protection: H

National Fire Protection Association (U.S.A.):

Health: 3

Flammability: 2

Reactivity: 0

Specific hazard:

Protective Equipment:

Gloves (impervious).

Synthetic apron.

Vapor respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate.

Splash goggles.

Section 16: Other Information

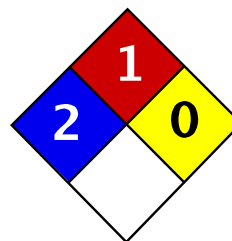
References: Not available.

Other Special Considerations: Not available.

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Last Updated: 11/06/2008 12:00 PM

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Health	2
Fire	1
Reactivity	0
Personal Protection	E

Material Safety Data Sheet

L-Cysteine HCl monohydrate MSDS

Section 1: Chemical Product and Company Identification

Product Name: L-Cysteine HCl monohydrate

Catalog Codes: SLC1114, SLC2905, SLC2695

CAS#: 7048-04-6

RTECS: HA2275000

TSCA: TSCA 8(b) inventory: L-Cysteine HCl monohydrate

CI#: Not available.

Synonym: 2-Amino-3-mercaptopropanoic acid hydrochloride

Chemical Formula: C3H7NO2S.HCl.H2O

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.

Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
{L-}Cysteine HCl monohydrate	7048-04-6	100

Toxicological Data on Ingredients: L-Cysteine HCl monohydrate: ORAL (LD50): Acute: 3550 mg/kg [Mouse]. 5580 mg/kg [Rat]. 4200 mg/kg [Mouse].

Section 3: Hazards Identification

Potential Acute Health Effects:

Very hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation. Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering.

Potential Chronic Health Effects:

Very hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation.

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Not available.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

Repeated or prolonged inhalation of dust may lead to chronic respiratory irritation.

Section 4: First Aid Measures

Eye Contact:

Check for and remove any contact lenses. Immediately flush eyes with running water for at least 15 minutes, keeping eyelids open. Cold water may be used. Do not use an eye ointment. Seek medical attention.

Skin Contact:

After contact with skin, wash immediately with plenty of water. Gently and thoroughly wash the contaminated skin with running water and non-abrasive soap. Be particularly careful to clean folds, crevices, creases and groin. Cold water may be used. Cover the irritated skin with an emollient. If irritation persists, seek medical attention. Wash contaminated clothing before reusing.

Serious Skin Contact:

Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek medical attention.

Inhalation: Allow the victim to rest in a well ventilated area. Seek immediate medical attention.

Serious Inhalation: Not available.

Ingestion:

Do not induce vomiting. Loosen tight clothing such as a collar, tie, belt or waistband. If the victim is not breathing, perform mouth-to-mouth resuscitation. Seek immediate medical attention.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: May be combustible at high temperature.

Auto-Ignition Temperature: Not available.

Flash Points: Not available.

Flammable Limits: Not available.

Products of Combustion:

These products are carbon oxides (CO, CO₂), nitrogen oxides (NO, NO₂...), sulfur oxides (SO₂, SO₃...), halogenated compounds.

Fire Hazards in Presence of Various Substances: Not available.

Explosion Hazards in Presence of Various Substances:

Risks of explosion of the product in presence of mechanical impact: Not available.

Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions:

SMALL FIRE: Use DRY chemical powder.

LARGE FIRE: Use water spray, fog or foam. Do not use water jet.

Special Remarks on Fire Hazards: Not available.

Special Remarks on Explosion Hazards: Not available.

Section 6: Accidental Release Measures

Small Spill:

Use appropriate tools to put the spilled solid in a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:

Use a shovel to put the material into a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and allow to evacuate through the sanitary system.

Section 7: Handling and Storage**Precautions:**

Keep away from heat. Keep away from sources of ignition. Empty containers pose a fire risk, evaporate the residue under a fume hood. Ground all equipment containing material. Do not ingest. Do not breathe dust. In case of insufficient ventilation, wear suitable respiratory equipment. If ingested, seek medical advice immediately and show the container or the label. Avoid contact with skin and eyes.

Storage:

Keep container dry. Keep in a cool place. Ground all equipment containing material. Keep container tightly closed. Keep in a cool, well-ventilated place. Combustible materials should be stored away from extreme heat and away from strong oxidizing agents.

Section 8: Exposure Controls/Personal Protection**Engineering Controls:**

Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection:

Splash goggles. Lab coat. Dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid. (Solid crystalline powder.)

Odor: Not available.

Taste: Not available.

Molecular Weight: 175.64 g/mole

Color: White.

pH (1% soln/water): Not available.

Boiling Point: Not available.

Melting Point: Decomposes. (176°C or 348.8°F)

Critical Temperature: Not available.

Specific Gravity: Not available.

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility: Soluble in cold water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Not available.

Incompatibility with various substances: Not available.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity: Not available.

Special Remarks on Corrosivity: Not available.

Polymerization: No.

Section 11: Toxicological Information

Routes of Entry: Eye contact. Inhalation. Ingestion.

Toxicity to Animals: Acute oral toxicity (LD50): 3550 mg/kg [Mouse].

Chronic Effects on Humans: Not available.

Other Toxic Effects on Humans: Very hazardous in case of skin contact (irritant), of ingestion, of inhalation.

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: Not available.

Special Remarks on other Toxic Effects on Humans: Not available.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are more toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: Not applicable.

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations: TSCA 8(b) inventory: L-Cysteine HCl monohydrate

Other Regulations: OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

Other Classifications:

WHMIS (Canada): Not controlled under WHMIS (Canada).

DSCL (EEC):

R38- Irritating to skin.

R41- Risk of serious damage to eyes.

HMIS (U.S.A.):

Health Hazard: 2

Fire Hazard: 1

Reactivity: 0

Personal Protection: E

National Fire Protection Association (U.S.A.):

Health: 2

Flammability: 1

Reactivity: 0

Specific hazard:

Protective Equipment:

Gloves.

Lab coat.

Dust respirator. Be sure to use an approved/certified respirator or equivalent.

Splash goggles.

Section 16: Other Information

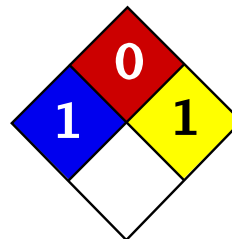
References: Not available.

Other Special Considerations: Not available.

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Health	1
Fire	0
Reactivity	0
Personal Protection	J

Material Safety Data Sheet

EDTA Disodium, 0.5 M Solution MSDS

Section 1: Chemical Product and Company Identification

Product Name: EDTA Disodium, 0.5 M Solution

Catalog Codes: SLE2083

CAS#: Mixture.

RTECS: Not applicable.

TSCA: TSCA 8(b) inventory: Sodium hydroxide; Water

CI#: Not applicable.

Synonym:

Chemical Name: Not applicable.

Chemical Formula: Not applicable.

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.

Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Edetate disodium, dihydrate	6381-92-6	18.6
Sodium hydroxide	1310-73-2	2
Water	7732-18-5	79.4

Toxicological Data on Ingredients: Sodium hydroxide LD50: Not available. LC50: Not available.

Section 3: Hazards Identification

Potential Acute Health Effects: Slightly hazardous in case of skin contact (irritant, permeator), of eye contact (irritant,), of ingestion.

Potential Chronic Health Effects:

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells. [Sodium hydroxide].

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

The substance may be toxic to mucous membranes, upper respiratory tract, skin, eyes.

Repeated or prolonged exposure to the substance can produce target organs damage.

Section 4: First Aid Measures

Eye Contact:

Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention.

Skin Contact:

In case of contact, immediately flush skin with plenty of water. Cover the irritated skin with an emollient. Remove contaminated clothing and shoes. Cold water may be used. Wash clothing before reuse. Thoroughly clean shoes before reuse. Get medical attention.

Serious Skin Contact: Not available.

Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

Serious Inhalation: Not available.

Ingestion:

Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. Loosen tight clothing such as a collar, tie, belt or waistband. Get medical attention if symptoms appear.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: Non-flammable.

Auto-Ignition Temperature: Not applicable.

Flash Points: Not applicable.

Flammable Limits: Not applicable.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances: Not applicable.

Explosion Hazards in Presence of Various Substances: Non-explosive in presence of open flames and sparks, of shocks.

Fire Fighting Media and Instructions: Not applicable.

Special Remarks on Fire Hazards: Not available.

Special Remarks on Explosion Hazards: Not Available

Section 6: Accidental Release Measures

Small Spill:

Dilute with water and mop up, or absorb with an inert dry material and place in an appropriate waste disposal container. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:

Absorb with an inert material and put the spilled material in an appropriate waste disposal. Finish cleaning by spreading water on the contaminated surface and allow to evacuate through the sanitary system. Be careful that the product is not present at a concentration level above TLV. Check TLV on the MSDS and with local authorities.

Section 7: Handling and Storage

Precautions:

Do not ingest. Do not breathe gas/fumes/ vapor/spray. Never add water to this product. If ingested, seek medical advice immediately and show the container or the label. Avoid contact with skin and eyes.

Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area.

Section 8: Exposure Controls/Personal Protection

Engineering Controls:

Provide exhaust ventilation or other engineering controls to keep the airborne concentrations of vapors below their respective threshold limit value.

Personal Protection: Splash goggles. Lab coat. Gloves.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Boots. Gloves. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits:

Sodium hydroxide

STEL: 2 (mg/m³) from ACGIH (TLV) [United States]

TWA: 2 CEIL: 2 (mg/m³) from OSHA (PEL) [United States]

CEIL: 2 (mg/m³) from NIOSH Consult local authorities for acceptable exposure limits.

Section 9: Physical and Chemical Properties

Physical state and appearance: Liquid.

Odor: Not available.

Taste: Not available.

Molecular Weight: Not applicable.

Color: Colorless.

pH (1% soln/water): pH of undiluted product: approx. 8 [Basic.]

Boiling Point: The lowest known value is 100°C (212°F) (Water).

Melting Point: Not available.

Critical Temperature: Not available.

Specific Gravity: Weighted average: 1.01 (Water = 1)

Vapor Pressure: The highest known value is 2.3 kPa (@ 20°C) (Water).

Vapor Density: The highest known value is 0.62 (Air = 1) (Water).

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility: Easily soluble in cold water, hot water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Incompatible materials

Incompatibility with various substances: Slightly reactive to reactive with oxidizing agents, reducing agents, metals, acids, alkalis.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity: No other information at this time. (Edetate disodium, dihydrate)

Special Remarks on Corrosivity: Not available.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Absorbed through skin. Eye contact.

Toxicity to Animals: Acute oral toxicity (LD50): >2000 mg/kg [Rat]. (Edetate disodium, dihydrate).

Chronic Effects on Humans:

MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells. [Sodium hydroxide].

Contains material which may cause damage to the following organs: mucous membranes, upper respiratory tract, skin, eyes.

Other Toxic Effects on Humans: Slightly hazardous in case of skin contact (irritant, permeator), of ingestion, of inhalation.

Special Remarks on Toxicity to Animals:

Lowest Published Lethal Dose:

LDL [Rabbit] - Route: Oral; Dose: 500 mg/kg (Sodium hydroxide)

Special Remarks on Chronic Effects on Humans:

Genetic (Mutation) Effects (Cytogenic Analysis)cited (dust inhalation in hamsters) in "Registry of Toxic Effects of Chemical Substances" (RTECS) database.

May cause adverse reproductive effects and birth defects (teratogenic) based on animal test data (Edetate disodium, dihydrate)

Special Remarks on other Toxic Effects on Humans:

Acute Potential Health Effects:

May irritate eyes, skin, respiratory tract, and mucous membranes.

Ingestion: It may cause gastrointestinal tract irritation with nausea, vomiting, and diarrhea. It may affect behavior/central nervous system (convulsions)

Chronic Potential Health Effects:

Ingestion: Prolonged or repeated ingestion may affect metabolism (weight loss), liver, urinary system.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The product itself and its products of degradation are not toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: Not applicable.

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations:

California prop. 65: This product contains the following ingredients for which the State of California has found to cause birth defects which would require a warning under the statute: No products were found.

California prop. 65: This product contains the following ingredients for which the State of California has found to cause cancer which would require a warning under the statute: No products were found.

Illinois toxic substances disclosure to employee act: Sodium hydroxide

Illinois chemical safety act: Sodium hydroxide

New York release reporting list: Sodium hydroxide

Rhode Island RTK hazardous substances: Sodium hydroxide

Pennsylvania RTK: Sodium hydroxide

Minnesota: Sodium hydroxide

Massachusetts RTK: Sodium hydroxide

New Jersey: Sodium hydroxide

Louisiana spill reporting: Sodium hydroxide

California Director's List of Hazardous Substances: Sodium Hydroxide

TSCA 8(b) inventory: Sodium hydroxide; Water

CERCLA: Hazardous substances.: Sodium hydroxide: 1000 lbs. (453.6 kg);

Other Regulations: OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

Other Classifications:

WHMIS (Canada): Not controlled under WHMIS (Canada).

DSCL (EEC):

R36/38- Irritating to eyes and skin.

S24/25- Avoid contact with skin and eyes.

S36/37/39- Wear suitable protective clothing, gloves and eye/face protection.

HMIS (U.S.A.):

Health Hazard: 1

Fire Hazard: 0

Reactivity: 0

Personal Protection: j

National Fire Protection Association (U.S.A.):

Health: 1

Flammability: 0

Reactivity: 1

Specific hazard:

Protective Equipment:

Gloves.

Lab coat.

Not applicable.

Splash goggles.

Section 16: Other Information

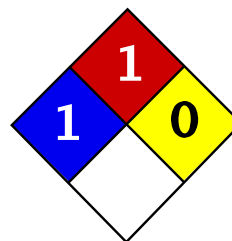
References: Not available.

Other Special Considerations: Not available.

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Last Updated: 11/06/2008 12:00 PM

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Health	1
Fire	1
Reactivity	0
Personal Protection	A

Material Safety Data Sheet

Dextrose anhydrous MSDS

Section 1: Chemical Product and Company Identification

Product Name: Dextrose anhydrous

Catalog Codes: SLD3880, SLD4483

CAS#: 50-99-7

RTECS: LZ6600000

TSCA: TSCA 8(b) inventory: Dextrose anhydrous

CI#: Not available.

Synonym: D-Glucose

Chemical Name: Not available.

Chemical Formula: C₆H₁₂O₆

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.

Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:

1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Dextrose anhydrous	50-99-7	100

Toxicological Data on Ingredients: Not applicable.

Section 3: Hazards Identification

Potential Acute Health Effects: Slightly hazardous in case of eye contact (irritant), of ingestion, of inhalation.

Potential Chronic Health Effects:

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Not available.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

Repeated or prolonged exposure is not known to aggravate medical condition.

Section 4: First Aid Measures

Eye Contact: Immediately flush eyes with running water for at least 15 minutes, keeping eyelids open. Cold water may be used.

Skin Contact: No known effect on skin contact, rinse with water for a few minutes.

Serious Skin Contact: Not available.

Inhalation: Allow the victim to rest in a well ventilated area. Seek immediate medical attention.

Serious Inhalation: Not available.

Ingestion:

Do not induce vomiting. Loosen tight clothing such as a collar, tie, belt or waistband. If the victim is not breathing, perform mouth-to-mouth resuscitation. Seek immediate medical attention.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: May be combustible at high temperature.

Auto-Ignition Temperature: Not available.

Flash Points: Not available.

Flammable Limits: Not available.

Products of Combustion: These products are carbon oxides (CO, CO₂).

Fire Hazards in Presence of Various Substances: Not available.

Explosion Hazards in Presence of Various Substances:

Risks of explosion of the product in presence of mechanical impact: Not available.

Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions:

SMALL FIRE: Use DRY chemical powder.

LARGE FIRE: Use water spray, fog or foam. Do not use water jet.

Special Remarks on Fire Hazards: Not available.

Special Remarks on Explosion Hazards: Not available.

Section 6: Accidental Release Measures

Small Spill:

Use appropriate tools to put the spilled solid in a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:

Use a shovel to put the material into a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and allow to evacuate through the sanitary system. Be careful that the product is not present at a concentration level above TLV. Check TLV on the MSDS and with local authorities.

Section 7: Handling and Storage

Precautions:

Keep away from heat. Keep away from sources of ignition. Empty containers pose a fire risk, evaporate the residue under a fume hood. Ground all equipment containing material. Do not ingest. Do not breathe dust. If ingested, seek medical advice immediately and show the container or the label.

Storage:

Keep container dry. Keep in a cool place. Ground all equipment containing material. Keep container tightly closed. Keep in a cool, well-ventilated place. Combustible materials should be stored away from extreme heat and away from strong oxidizing agents.

Section 8: Exposure Controls/Personal Protection

Engineering Controls:

Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection: Safety glasses. Lab coat.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Boots. Gloves. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits:

TWA: 300 (ppm)

Consult local authorities for acceptable exposure limits.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid.

Odor: Not available.

Taste: Not available.

Molecular Weight: 180.16 g/mole

Color: Not available.

pH (1% soln/water): Not available.

Boiling Point: Decomposes.

Melting Point: 146°C (294.8°F)

Critical Temperature: Not available.

Specific Gravity: 1.562 (Water = 1)

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility: Easily soluble in cold water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Not available.

Incompatibility with various substances: Not available.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity: Not available.

Special Remarks on Corrosivity: Not available.

Polymerization: No.

Section 11: Toxicological Information

Routes of Entry: Not available.

Toxicity to Animals: Acute oral toxicity (LD50): 25800 mg/kg [Rat].

Chronic Effects on Humans: Not available.

Other Toxic Effects on Humans: Slightly hazardous in case of ingestion, of inhalation.

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: Passes through the placental barrier in human.

Special Remarks on other Toxic Effects on Humans: Not available.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are more toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: Not applicable.

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations: TSCA 8(b) inventory: Dextrose anhydrous

Other Regulations: Not available..

Other Classifications:

WHMIS (Canada): Not controlled under WHMIS (Canada).

DSCL (EEC):

This product is not classified according to the EU regulations.

HMIS (U.S.A.):

Health Hazard: 1

Fire Hazard: 1

Reactivity: 0

Personal Protection: a

National Fire Protection Association (U.S.A.):

Health: 1

Flammability: 1

Reactivity: 0

Specific hazard:

Protective Equipment:

Not applicable.

Lab coat.

Not applicable.

Safety glasses.

Section 16: Other Information

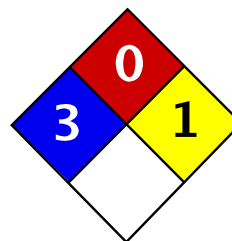
References: Not available.

Other Special Considerations: Not available.

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Health	3
Fire	0
Reactivity	1
Personal Protection	

Material Safety Data Sheet

Hydrochloric acid MSDS

Section 1: Chemical Product and Company Identification

Product Name: Hydrochloric acid

Catalog Codes: SLH1462, SLH3154

CAS#: Mixture.

RTECS: MW4025000

TSCA: TSCA 8(b) inventory: Hydrochloric acid

CI#: Not applicable.

Synonym: Hydrochloric Acid; Muriatic Acid

Chemical Name: Not applicable.

Chemical Formula: Not applicable.

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.

Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:

1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Hydrogen chloride	7647-01-0	20-38
Water	7732-18-5	62-80

Toxicological Data on Ingredients: Hydrogen chloride: GAS (LC50): Acute: 4701 ppm 0.5 hours [Rat].

Section 3: Hazards Identification

Potential Acute Health Effects:

Very hazardous in case of skin contact (corrosive, irritant, permeator), of eye contact (irritant, corrosive), of ingestion, . Slightly hazardous in case of inhalation (lung sensitizer). Non-corrosive for lungs. Liquid or spray mist may produce tissue damage particularly on mucous membranes of eyes, mouth and respiratory tract. Skin contact may produce burns. Inhalation of the spray mist may produce severe irritation of respiratory tract, characterized by coughing, choking, or shortness of breath. Severe over-exposure can result in death. Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering.

Potential Chronic Health Effects:

Slightly hazardous in case of skin contact (sensitizer).

CARCINOGENIC EFFECTS: Classified 3 (Not classifiable for human.) by IARC [Hydrochloric acid].

MUTAGENIC EFFECTS: Not available.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

The substance may be toxic to kidneys, liver, mucous membranes, upper respiratory tract, skin, eyes, Circulatory System, teeth.

Repeated or prolonged exposure to the substance can produce target organs damage. Repeated or prolonged contact with spray mist may produce chronic eye irritation and severe skin irritation. Repeated or prolonged exposure to spray mist may produce respiratory tract irritation leading to frequent attacks of bronchial infection. Repeated exposure to a highly toxic material may produce general deterioration of health by an accumulation in one or many human organs.

Section 4: First Aid Measures

Eye Contact:

Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention immediately.

Skin Contact:

In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Cover the irritated skin with an emollient. Cold water may be used. Wash clothing before reuse. Thoroughly clean shoes before reuse. Get medical attention immediately.

Serious Skin Contact:

Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek immediate medical attention.

Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.

Serious Inhalation:

Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. If breathing is difficult, administer oxygen. If the victim is not breathing, perform mouth-to-mouth resuscitation. WARNING: It may be hazardous to the person providing aid to give mouth-to-mouth resuscitation when the inhaled material is toxic, infectious or corrosive. Seek immediate medical attention.

Ingestion:

If swallowed, do not induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. Loosen tight clothing such as a collar, tie, belt or waistband. Get medical attention immediately.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: Non-flammable.

Auto-Ignition Temperature: Not applicable.

Flash Points: Not applicable.

Flammable Limits: Not applicable.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances: of metals

Explosion Hazards in Presence of Various Substances: Non-explosive in presence of open flames and sparks, of shocks.

Fire Fighting Media and Instructions: Not applicable.

Special Remarks on Fire Hazards:

Non combustible.

Calcium carbide reacts with hydrogen chloride gas with incandescence.

Uranium phosphide reacts with hydrochloric acid to release spontaneously flammable phosphine.

Rubidium acetylene carbides burns with slightly warm hydrochloric acid.

Lithium silicide in contact with hydrogen chloride becomes incandescent. When dilute hydrochloric acid is used, gas spontaneously flammable in air is evolved.

Magnesium boride treated with concentrated hydrochloric acid produces spontaneously flammable gas.

Cesium acetylene carbide burns hydrogen chloride gas.

Cesium carbide ignites in contact with hydrochloric acid unless acid is dilute.

Reacts with most metals to produce flammable Hydrogen gas.

Special Remarks on Explosion Hazards:

Hydrogen chloride in contact with the following can cause an explosion, ignition on contact, or other

violent/vigorous reaction: Acetic anhydride $\text{AgClO} + \text{CCl}_4$ Alcohols + hydrogen cyanide, Aluminum

Aluminum-titanium alloys (with HCl vapor), 2-Amino ethanol, Ammonium hydroxide, Calcium carbide Ca_3P_2

Chlorine + dinitroanilines (evolves gas), Chlorosulfonic acid Cesium carbide Cesium acetylene carbide,

1,1-Difluoroethylene Ethylene diamine Ethylene imine, Fluorine, HClO_4 Hexalithium disilicide H_2SO_4 Metal

acetylides or carbides, Magnesium boride, Mercuric sulfate, Oleum, Potassium permanganate,

beta-Propiolactone Propylene oxide Rubidium carbide, Rubidium, acetylene carbide Sodium (with aqueous HCl),

Sodium hydroxide Sodium tetraselenium, Sulfonic acid, Tetraselenium tetranitride, U_3P_4 , Vinyl acetate.

Silver perchlorate with carbon tetrachloride in the presence of hydrochloric acid produces trichloromethyl

perchlorate which detonates at 40 deg. C.

Section 6: Accidental Release Measures**Small Spill:**

Dilute with water and mop up, or absorb with an inert dry material and place in an appropriate waste disposal container. If necessary: Neutralize the residue with a dilute solution of sodium carbonate.

Large Spill:

Corrosive liquid. Poisonous liquid.

Stop leak if without risk. Absorb with DRY earth, sand or other non-combustible material. Do not get water inside container. Do not touch spilled material. Use water spray curtain to divert vapor drift. Use water spray to reduce vapors. Prevent entry into sewers, basements or confined areas; dike if needed. Call for assistance on disposal.

Neutralize the residue with a dilute solution of sodium carbonate. Be careful that the product is not present at a concentration level above TLV. Check TLV on the MSDS and with local authorities.

Section 7: Handling and Storage**Precautions:**

Keep locked up.. Keep container dry. Do not ingest. Do not breathe gas/fumes/ vapor/spray. Never add water to this product. In case of insufficient ventilation, wear suitable respiratory equipment. If ingested, seek medical advice immediately and show the container or the label. Avoid contact with skin and eyes. Keep away from incompatibles such as oxidizing agents, organic materials, metals, alkalis, moisture.

May corrode metallic surfaces. Store in a metallic or coated fiberboard drum using a strong polyethylene inner package.

Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area.

Section 8: Exposure Controls/Personal Protection**Engineering Controls:**

Provide exhaust ventilation or other engineering controls to keep the airborne concentrations of vapors below their respective threshold limit value. Ensure that eyewash stations and safety showers are proximal to the work-station location.

Personal Protection:

Face shield. Full suit. Vapor respirator. Be sure to use an approved/certified respirator or equivalent. Gloves. Boots.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Vapor respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits:

CEIL: 5 (ppm) from OSHA (PEL) [United States]

CEIL: 7 (mg/m3) from OSHA (PEL) [United States]

CEIL: 5 from NIOSH

CEIL: 7 (mg/m3) from NIOSH

TWA: 1 STEL: 5 (ppm) [United Kingdom (UK)]

TWA: 2 STEL: 8 (mg/m3) [United Kingdom (UK)] Consult local authorities for acceptable exposure limits.

Section 9: Physical and Chemical Properties

Physical state and appearance: Liquid.

Odor: Pungent. Irritating (Strong.)

Taste: Not available.

Molecular Weight: Not applicable.

Color: Colorless to light yellow.

pH (1% soln/water): Acidic.

Boiling Point:

108.58 C @ 760 mm Hg (for 20.22% HCl in water)

83 C @ 760 mm Hg (for 31% HCl in water)

50.5 C (for 37% HCl in water)

Melting Point:

-62.25°C (-80°F) (20.69% HCl in water)

-46.2 C (31.24% HCl in water)

-25.4 C (39.17% HCl in water)

Critical Temperature: Not available.

Specific Gravity:

1.1- 1.19 (Water = 1)

1.10 (20% and 22% HCl solutions)

1.12 (24% HCl solution)

1.15 (29.57% HCl solution)

1.16 (32% HCl solution)

1.19 (37% and 38% HCl solutions)

Vapor Pressure: 16 kPa (@ 20°C) average

Vapor Density: 1.267 (Air = 1)

Volatility: Not available.

Odor Threshold: 0.25 to 10 ppm

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water, diethyl ether.

Solubility: Soluble in cold water, hot water, diethyl ether.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Incompatible materials, water

Incompatibility with various substances:

Highly reactive with metals.

Reactive with oxidizing agents, organic materials, alkalis, water.

Corrosivity:

Extremely corrosive in presence of aluminum, of copper, of stainless steel(304), of stainless steel(316).

Non-corrosive in presence of glass.

Special Remarks on Reactivity:

Reacts with water especially when water is added to the product.

Absorption of gaseous hydrogen chloride on mercuric sulfate becomes violent @ 125 deg. C.

Sodium reacts very violently with gaseous hydrogen chloride.

Calcium phosphide and hydrochloric acid undergo very energetic reaction.

It reacts with oxidizers releasing chlorine gas.

Incompatible with, alkali metals, carbides, borides, metal oxides, vinyl acetate, acetylides, sulphides, phosphides, cyanides, carbonates.

Reacts with most metals to produce flammable Hydrogen gas.

Reacts violently (moderate reaction with heat of evolution) with water especially when water is added to the product. Isolate hydrogen chloride from heat, direct sunlight, alkalies (reacts vigorously), organic materials, and oxidizers (especially nitric acid and chlorates), amines, metals, copper and alloys (e.g. brass), hydroxides, zinc (galvanized materials), lithium silicide (incandescence), sulfuric acid(increase in temperature and pressure)

Hydrogen chloride gas is emitted when this product is in contact with sulfuric acid.

Adsorption of Hydrochloric Acid onto silicon dioxide results in exothermic reaction.

Hydrogen chloride causes aldehydes and epoxides to violently polymerize.

Hydrogen chloride or Hydrochloric Acid in contact with the following can cause explosion or ignition on contact or

Special Remarks on Corrosivity:

Highly corrosive. Incompatible with copper and copper alloys. It attacks nearly all metals (mercury, gold, platinum, tantalum, silver, and certain alloys are exceptions).

It is one of the most corrosive of the nonoxidizing acids in contact with copper alloys.

No corrosivity data on zinc, steel.

Severe Corrosive effect on brass and bronze

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Absorbed through skin. Dermal contact. Eye contact. Inhalation.

Toxicity to Animals:

Acute oral toxicity (LD50): 900 mg/kg [Rabbit].

Acute toxicity of the vapor (LC50): 1108 ppm, 1 hours [Mouse].

Acute toxicity of the vapor (LC50): 3124 ppm, 1 hours [Rat].

Chronic Effects on Humans:

CARCINOGENIC EFFECTS: Classified 3 (Not classifiable for human.) by IARC [Hydrochloric acid].

May cause damage to the following organs: kidneys, liver, mucous membranes, upper respiratory tract, skin,

eyes, Circulatory System, teeth.

Other Toxic Effects on Humans:

Very hazardous in case of skin contact (corrosive, irritant, permeator), of ingestion, .
Hazardous in case of eye contact (corrosive), of inhalation (lung corrosive).

Special Remarks on Toxicity to Animals:

Lowest Published Lethal Doses (LDL/LCL)

LDL [Man] -Route: Oral; 2857 ug/kg

LCL [Human] - Route: Inhalation; Dose: 1300 ppm/30M

LCL [Rabbit] - Route: Inhalation; Dose: 4413 ppm/30M

Special Remarks on Chronic Effects on Humans:

May cause adverse reproductive effects (fetotoxicity).

May affect genetic material.

Special Remarks on other Toxic Effects on Humans:

Acute Potential Health Effects:

Skin: Corrosive. Causes severe skin irritation and burns.

Eyes: Corrosive. Causes severe eye irritation/conjunctivitis, burns, corneal necrosis.

Inhalation: May be fatal if inhaled. Material is extremely destructive to tissue of the mucous membranes and upper respiratory tract. Inhalation of hydrochloric acid fumes produces nose, throat, and laryngeal burning, and irritation, pain and inflammation, coughing, sneezing, choking sensation, hoarseness, laryngeal spasms, upper respiratory tract edema, chest pains, as well as headache, and palpitations. Inhalation of high concentrations can result in corrosive burns, necrosis of bronchial epithelium, constriction of the larynx and bronchi, nasospetal perforation, glottal closure,

occur, particularly if exposure is prolonged. May affect the liver.

Ingestion: May be fatal if swallowed. Causes irritation and burning, ulceration, or perforation of the gastrointestinal tract and resultant peritonitis, gastric hemorrhage and infection. Can also cause nausea, vomiting (with "coffee ground" emesis), diarrhea, thirst, difficulty swallowing, salivation, chills, fever, uneasiness, shock, strictures and stenosis (esophageal, gastric, pyloric). May affect behavior (excitement), the cardiovascular system (weak rapid pulse, tachycardia), respiration (shallow respiration), and urinary system (kidneys- renal failure, nephritis).

Acute exposure via inhalation or ingestion can also cause erosion of tooth enamel.

Chronic Potential Health Effects:

dyspnea, bronchitis. Chemical pneumonitis and pulmonary edema can also

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are less toxic than the product itself.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Class 8: Corrosive material

Identification: : Hydrochloric acid, solution UNNA: 1789 PG: II

Special Provisions for Transport: Not available.

Section 15: Other Regulatory Information

Federal and State Regulations:

Connecticut hazardous material survey.: Hydrochloric acid
Illinois toxic substances disclosure to employee act: Hydrochloric acid
Illinois chemical safety act: Hydrochloric acid
New York release reporting list: Hydrochloric acid
Rhode Island RTK hazardous substances: Hydrochloric acid
Pennsylvania RTK: Hydrochloric acid
Minnesota: Hydrochloric acid
Massachusetts RTK: Hydrochloric acid
Massachusetts spill list: Hydrochloric acid
New Jersey: Hydrochloric acid
New Jersey spill list: Hydrochloric acid
Louisiana RTK reporting list: Hydrochloric acid
Louisiana spill reporting: Hydrochloric acid
California Director's List of Hazardous Substances: Hydrochloric acid
TSCA 8(b) inventory: Hydrochloric acid
TSCA 4(a) proposed test rules: Hydrochloric acid
SARA 302/304/311/312 extremely hazardous substances: Hydrochloric acid
SARA 313 toxic chemical notification and release reporting: Hydrochloric acid
CERCLA: Hazardous substances.: Hydrochloric acid: 5000 lbs. (2268 kg)

Other Regulations:

OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).
EINECS: This product is on the European Inventory of Existing Commercial Chemical Substances.

Other Classifications:

WHMIS (Canada):

CLASS D-2A: Material causing other toxic effects (VERY TOXIC).
CLASS E: Corrosive liquid.

DSCL (EEC):

R34- Causes burns.
R37- Irritating to respiratory system.
S26- In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
S45- In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).

HMIS (U.S.A.):

Health Hazard: 3

Fire Hazard: 0

Reactivity: 1

Personal Protection:

National Fire Protection Association (U.S.A.):

Health: 3

Flammability: 0

Reactivity: 1

Specific hazard:

Protective Equipment:

Gloves.

Full suit.

Vapor respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate.

Face shield.

Section 16: Other Information

References:

-Hawley, G.G.. The Condensed Chemical Dictionary, 11e ed., New York N.Y., Van Nostrand Reinold, 1987.

-SAX, N.I. Dangerous Properties of Industrial Materials. Toronto, Van Nostrand Reinold, 6e ed. 1984.

-The Sigma-Aldrich Library of Chemical Safety Data, Edition II.

-Guide de la loi et du règlement sur le transport des marchandises dangereuses au Canada. Centre de conformité international Ltée. 1986.

Other Special Considerations: Not available.

Created: 10/09/2005 05:45 PM

Last Updated: 10/09/2005 05:45 PM

The information above is believed to be accurate and represents the best information currently available to us. However, we make no warranty of merchantability or any other warranty, express or implied, with respect to such information, and we assume no liability resulting from its use. Users should make their own investigations to determine the suitability of the information for their particular purposes. In no event shall ScienceLab.com be liable for any claims, losses, or damages of any third party or for lost profits or any special, indirect, incidental, consequential or exemplary damages, howsoever arising, even if ScienceLab.com has been advised of the possibility of such damages.

Material Safety Data Sheet

Thermo
SCIENTIFIC

Immobilized Papain

1. Product and company identification

Product name	: Immobilized Papain		
Supplier	: Thermo Fisher Scientific Pierce Biotechnology P.O. Box 117 Rockford, IL 61105 United States 815.968.0747 or 800.874.3723	Manufacturer	: Thermo Fisher Scientific Pierce Biotechnology P.O. Box 117 Rockford, IL 61105 United States 815.968.0747 800.874.3723
Product No.	: 0020341 1861442 1851456 1901714		
MSDS #	: 0100		
Validation date	: 6/2/2008.		
Print date	: 6/2/2008.		
Responsible name	: MSDS (Regulatory Affairs)		
<u>In case of emergency</u>	: CHEMTREC: 800.424.9300 OUTSIDE US: 202.483.7616	<u>Use of Substance/Preparation</u>	: Refer to the instruction booklet for proper and intended use. Otherwise, contact supplier for specific applications.

2. Hazards identification

Physical state	: Liquid. [Suspension.]
OSHA/HCS status	: This material is considered hazardous by the OSHA Hazard Communication Standard (29 CFR 1910.1200).
Emergency overview	: WARNING ! CAUSES RESPIRATORY TRACT, EYE AND SKIN IRRITATION. CONTAINS MATERIAL THAT CAN CAUSE TARGET ORGAN DAMAGE. Irritating to eyes, respiratory system and skin. Avoid exposure - obtain special instructions before use. Do not breathe vapor or mist. Avoid contact with eyes, skin and clothing. Contains material that can cause target organ damage. Use only with adequate ventilation. Keep container tightly closed and sealed until ready for use. Wash thoroughly after handling.
Routes of entry	: Eye contact. Inhalation. Ingestion.
<u>Potential acute health effects</u>	
Inhalation	: Irritating to respiratory system.
Ingestion	: No known significant effects or critical hazards.
Skin	: Irritating to skin.
Eyes	: Irritating to eyes.
<u>Potential chronic health effects</u>	
Chronic effects	: Contains material that can cause target organ damage.
Carcinogenicity	: No known significant effects or critical hazards.
Mutagenicity	: No known significant effects or critical hazards.
Teratogenicity	: No known significant effects or critical hazards.
Developmental effects	: No known significant effects or critical hazards.
Fertility effects	: No known significant effects or critical hazards.
Target organs	: Contains material which may cause damage to the following organs: kidneys, upper respiratory tract, skin, eye, lens or cornea.
<u>Over-exposure signs/symptoms</u>	

2. Hazards identification

Inhalation	: Adverse symptoms may include the following: respiratory tract irritation coughing
Ingestion	: No specific data.
Skin	: Adverse symptoms may include the following: irritation redness
Eyes	: Adverse symptoms may include the following: pain or irritation watering redness
Medical conditions aggravated by over-exposure	: Pre-existing disorders involving any target organs mentioned in this MSDS as being at risk may be aggravated by over-exposure to this product.

The preparation is classified as dangerous according to Directive 1999/45/EC and its amendments.

Classification	: Xi; R36/37/38
Human health hazards	: Irritating to eyes, respiratory system and skin.
See toxicological information (section 11)	

3. Composition/information on ingredients

United States

<u>Name</u>	<u>CAS number</u>	<u>%</u>
Glycerol	56-81-5	20 - 25

Europe

Substance/preparation : Preparation

<u>Ingredient name</u>	<u>CAS number</u>	<u>%</u>	<u>EC number</u>	<u>Classification</u>
Glycerol	56-81-5	20 - 25	200-289-5	Xi; R36/37/38 [1] [2]

There are no ingredients or additional ingredients present which, within the current knowledge of the supplier and in the concentrations applicable, are classified as hazardous to health or the environment and hence require reporting in this section.

[1] Substance classified with a health or environmental hazard

[2] Substance with a workplace exposure limit

Occupational exposure limits, if available, are listed in section 8.

4. First aid measures

Inhalation	: Move exposed person to fresh air. If it is suspected that fumes are still present, the rescuer should wear an appropriate mask or self-contained breathing apparatus. Keep person warm and at rest. If not breathing, if breathing is irregular or if respiratory arrest occurs, provide artificial respiration or oxygen by trained personnel. It may be dangerous to the person providing aid to give mouth-to-mouth resuscitation. Get medical attention. If unconscious, place in recovery position and get medical attention immediately. Maintain an open airway. Loosen tight clothing such as a collar, tie, belt or waistband.
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4 . First aid measures

- Ingestion** : Wash out mouth with water. Remove dentures if any. Move exposed person to fresh air. Keep person warm and at rest. If material has been swallowed and the exposed person is conscious, give small quantities of water to drink. Stop if the exposed person feels sick as vomiting may be dangerous. Do not induce vomiting unless directed to do so by medical personnel. If vomiting occurs, the head should be kept low so that vomit does not enter the lungs. Get medical attention. Never give anything by mouth to an unconscious person. If unconscious, place in recovery position and get medical attention immediately. Maintain an open airway. Loosen tight clothing such as a collar, tie, belt or waistband.
- Skin contact** : Flush contaminated skin with plenty of water. Remove contaminated clothing and shoes. Continue to rinse for at least 10 minutes. Get medical attention. Wash clothing before reuse. Clean shoes thoroughly before reuse.
- Eye contact** : Immediately flush eyes with plenty of water for at least 15 minutes, occasionally lifting the upper and lower eyelids. Check for and remove any contact lenses. Get medical attention.
- Protection of first-aiders** : No action shall be taken involving any personal risk or without suitable training. If it is suspected that fumes are still present, the rescuer should wear an appropriate mask or self-contained breathing apparatus. It may be dangerous to the person providing aid to give mouth-to-mouth resuscitation.

See section 11 for more detailed information on health effects and symptoms.

5 . Fire-fighting measures

- Flammability of the product** : In a fire or if heated, a pressure increase will occur and the container may burst.
- Extinguishing media**
- Suitable** : Use an extinguishing agent suitable for the surrounding fire.
- Not suitable** : None known.
- Special exposure hazards** : Promptly isolate the scene by removing all persons from the vicinity of the incident if there is a fire. No action shall be taken involving any personal risk or without suitable training.
- Hazardous combustion products** : Decomposition products may include the following materials:
carbon oxides
- Special protective equipment for fire-fighters** : Fire-fighters should wear appropriate protective equipment and self-contained breathing apparatus (SCBA) with a full face-piece operated in positive pressure mode.

6 . Accidental release measures

- Personal precautions** : No action shall be taken involving any personal risk or without suitable training. Evacuate surrounding areas. Keep unnecessary and unprotected personnel from entering. Do not touch or walk through spilled material. Avoid breathing vapor or mist. Provide adequate ventilation. Wear appropriate respirator when ventilation is inadequate. Put on appropriate personal protective equipment (see section 8).
- Environmental precautions** : Avoid dispersal of spilled material and runoff and contact with soil, waterways, drains and sewers. Inform the relevant authorities if the product has caused environmental pollution (sewers, waterways, soil or air).
- Large spill** : Stop leak if without risk. Move containers from spill area. Approach release from upwind. Prevent entry into sewers, water courses, basements or confined areas. Wash spillages into an effluent treatment plant or proceed as follows. Contain and collect spillage with non-combustible, absorbent material e.g. sand, earth, vermiculite or diatomaceous earth and place in container for disposal according to local regulations (see section 13). Dispose of via a licensed waste disposal contractor. Contaminated absorbent material may pose the same hazard as the spilled product. Note: see section 1 for emergency contact information and section 13 for waste disposal.

6 . Accidental release measures

- Small spill** : Stop leak if without risk. Move containers from spill area. Dilute with water and mop up if water-soluble or absorb with an inert dry material and place in an appropriate waste disposal container. Dispose of via a licensed waste disposal contractor.

7 . Handling and storage

- Handling** : Put on appropriate personal protective equipment (see section 8). Eating, drinking and smoking should be prohibited in areas where this material is handled, stored and processed. Workers should wash hands and face before eating, drinking and smoking. Do not get in eyes or on skin or clothing. Do not breathe vapor or mist. Do not ingest. Use only with adequate ventilation. Wear appropriate respirator when ventilation is inadequate. Keep in the original container or an approved alternative made from a compatible material, kept tightly closed when not in use. Empty containers retain product residue and can be hazardous. Do not reuse container.

- Storage** : Store between the following temperatures: 2 to 8°C (35.6 to 46.4°F). Store in accordance with local regulations. Store in original container protected from direct sunlight in a dry, cool and well-ventilated area, away from incompatible materials (see section 10) and food and drink. Keep container tightly closed and sealed until ready for use. Containers that have been opened must be carefully resealed and kept upright to prevent leakage. Do not store in unlabeled containers. Use appropriate containment to avoid environmental contamination.

8 . Exposure controls/personal protection

Product name

United States

glycerin

Exposure limits

ACGIH (United States).

TWA: 10 mg/m³

ACGIH TLV (United States).

TWA: 10 mg/m³ 8 hour(s). Form: Total particulates

OSHA PEL (United States).

TWA: 15 mg/m³ 8 hour(s). Form: Total dust

ACGIH TLV (United States, 1/2007).

TWA: 10 mg/m³ 8 hour(s). Form: Mist

OSHA PEL (United States, 11/2006).

TWA: 5 mg/m³ 8 hour(s). Form: Respirable fraction

TWA: 15 mg/m³ 8 hour(s). Form: Total dust

OSHA PEL 1989 (United States, 3/1989).

TWA: 5 mg/m³ 8 hour(s). Form: Respirable fraction

TWA: 10 mg/m³ 8 hour(s). Form: Total dust

ACGIH TLV (United States).

TWA: 10 mg/m³ 8 hour(s). Form: Total particulates

OSHA PEL (United States).

TWA: 15 mg/m³ 8 hour(s). Form: Total dust

OSHA PEL (United States). Notes: Respirable

TWA: 15 mg/m³ 8 hour(s).

Europe

glycerin

ACGIH (United States).

TWA: 10 mg/m³

ACGIH TLV (United States).

TWA: 10 mg/m³ 8 hour(s). Form: Total particulates

TWA: 10 mg/m³ 8 hour(s). Form: Mist

TWA: 10 mg/m³ 8 hour(s). Form: Total particulates

Consult local authorities for acceptable exposure limits.

- Recommended monitoring procedures** : If this product contains ingredients with exposure limits, personal, workplace atmosphere or biological monitoring may be required to determine the effectiveness of the ventilation or other control measures and/or the necessity to use respiratory protective equipment.

8 . Exposure controls/personal protection

- Engineering measures** : Use only with adequate ventilation. If user operations generate dust, fumes, gas, vapor or mist, use process enclosures, local exhaust ventilation or other engineering controls to keep worker exposure to airborne contaminants below any recommended or statutory limits.
- Hygiene measures** : Wash hands, forearms and face thoroughly after handling chemical products, before eating, smoking and using the lavatory and at the end of the working period. Appropriate techniques should be used to remove potentially contaminated clothing. Wash contaminated clothing before reusing. Ensure that eyewash stations and safety showers are close to the workstation location.
- Personal protection**
- Respiratory** : Use a properly fitted, air-purifying or air-fed respirator complying with an approved standard if a risk assessment indicates this is necessary. Respirator selection must be based on known or anticipated exposure levels, the hazards of the product and the safe working limits of the selected respirator.
- Hands** : Chemical-resistant, impervious gloves complying with an approved standard should be worn at all times when handling chemical products if a risk assessment indicates this is necessary.
- Eyes** : Safety eyewear complying with an approved standard should be used when a risk assessment indicates this is necessary to avoid exposure to liquid splashes, mists, gases or dusts.
- Skin** : Personal protective equipment for the body should be selected based on the task being performed and the risks involved and should be approved by a specialist before handling this product.
- Environmental exposure controls** : Emissions from ventilation or work process equipment should be checked to ensure they comply with the requirements of environmental protection legislation. In some cases, fume scrubbers, filters or engineering modifications to the process equipment will be necessary to reduce emissions to acceptable levels.

9 . Physical and chemical properties

- Physical state** : Liquid. [Suspension.]
- Color** : White.
- pH** : 4.4
- Dispersibility properties** : Easily dispersible in the following materials: cold water and hot water.

10 . Stability and reactivity

- Chemical stability** : The product is stable. Under normal conditions of storage and use, hazardous polymerization will not occur.
- Conditions to avoid** : No specific data.
- Incompatible materials** : No specific data.
- Hazardous decomposition products** : Under normal conditions of storage and use, hazardous decomposition products should not be produced.
- Possibility of hazardous reactions** : Will not occur.

11 . Toxicological information

United States

Acute toxicity

Product/ingredient name	Result	Species	Dose	Exposure
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11 . Toxicological information

glycerin	LD50 Dermal	Rabbit	>10 g/kg	-
	LD50 Intraperitoneal	Rat	4420 mg/kg	-
	LD50 Intravenous	Rat	5566 mg/kg	-
	LD50 Oral	Rat	12600 mg/kg	-
	LD50 Oral	Rat	12600 mg/kg	-
	LD50 Oral	Mouse	4090 mg/kg	-
	LD50 Subcutaneous	Rat	100 mg/kg	-
	LDLo Intramuscular	Rat	10 mg/kg	-
	TDLo Intramuscular	Rat	8 mL/kg	-
	TDLo Intramuscular	Rat	5000 mg/kg	-

Conclusion/Summary : Not available.

Chronic toxicity

Conclusion/Summary : Not available.

Carcinogenicity

Conclusion/Summary : Not available.

Classification

Product/ingredient name	ACGIH	IARC	EPA	NIOSH	NTP	OSHA
glycerin	-	-	-	-	-	None.

Mutagenicity

Conclusion/Summary : Not available.

Teratogenicity

Conclusion/Summary : Not available.

Reproductive toxicity

Conclusion/Summary : Not available.

Europe

Chronic effects : No known significant effects or critical hazards.

Carcinogenicity : No known significant effects or critical hazards.

Mutagenicity : No known significant effects or critical hazards.

Teratogenicity : No known significant effects or critical hazards.

Developmental effects : No known significant effects or critical hazards.

Fertility effects : No known significant effects or critical hazards.

12 . Ecological information

Environmental effects : No known significant effects or critical hazards.

United States

Aquatic ecotoxicity

Conclusion/Summary : Not available.

Other adverse effects : No known significant effects or critical hazards.

13 . Disposal considerations

- Waste disposal** : The generation of waste should be avoided or minimized wherever possible. Dispose of surplus and non-recyclable products via a licensed waste disposal contractor. Disposal of this product, solutions and any by-products should at all times comply with the requirements of environmental protection and waste disposal legislation and any regional local authority requirements. Avoid dispersal of spilled material and runoff and contact with soil, waterways, drains and sewers.
- Hazardous waste** : The classification of the product may meet the criteria for a hazardous waste.
- Disposal should be in accordance with applicable regional, national and local laws and regulations.
- Refer to Section 7: HANDLING AND STORAGE and Section 8: EXPOSURE CONTROLS/PERSONAL PROTECTION for additional handling information and protection of employees.

14 . Transport information

Regulatory information	UN number	Proper shipping name	Classes	PG*
DOT Classification	Not regulated.	-	-	-
IATA-DGR Class	Not available.	Not available.	Not available.	-

PG* : Packing group

15 . Regulatory information

United States

- HCS Classification** : Irritating material
Target organ effects
- U.S. Federal regulations** : **United States inventory (TSCA 8b)**: All components are listed or exempted.
SARA 302/304/311/312 extremely hazardous substances: No products were found.
SARA 302/304 emergency planning and notification: No products were found.
SARA 302/304/311/312 hazardous chemicals: glycerin
SARA 311/312 MSDS distribution - chemical inventory - hazard identification: glycerin: Immediate (acute) health hazard, Delayed (chronic) health hazard
Clean Water Act (CWA) 307: No products were found.
Clean Water Act (CWA) 311: No products were found.
Clean Air Act (CAA) 112 accidental release prevention: No products were found.
Clean Air Act (CAA) 112 regulated flammable substances: No products were found.
Clean Air Act (CAA) 112 regulated toxic substances: No products were found.

Canada

- WHMIS (Canada)** : Class D-2B: Material causing other toxic effects (Toxic).
- Canadian lists** : **CEPA Toxic substances**: None of the components are listed.
Canadian ARET: None of the components are listed.
Canadian NPRI: None of the components are listed.
Alberta Designated Substances: None of the components are listed.
Ontario Designated Substances: None of the components are listed.
Quebec Designated Substances: None of the components are listed.
- Canada inventory** : **Canada inventory**: At least one component is not listed.

EU regulations

- Hazard symbol or symbols** :



15 . Regulatory information

Risk phrases : Irritant
: R36/37/38- Irritating to eyes, respiratory system and skin.
:

International regulations

International lists : **Australia inventory (AICS)**: All components are listed or exempted.
China inventory (IECSC): All components are listed or exempted.
Korea inventory (KECI): All components are listed or exempted.
Philippines inventory (PICCS): All components are listed or exempted.
Japan inventory (ENCS): Not determined.

16 . Other information

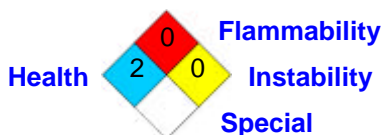
Label requirements : CAUSES RESPIRATORY TRACT, EYE AND SKIN IRRITATION. CONTAINS MATERIAL THAT CAN CAUSE TARGET ORGAN DAMAGE.

Hazardous Material Information System (U.S.A.) :

Health	2
Flammability	0
Physical hazards	0

The customer is responsible for determining the PPE code for this material.

National Fire Protection Association (U.S.A.) :



Date of printing : 6/2/2008.
Date of issue : 6/2/2008.
Date of previous issue : No previous validation.
Version : 1

 Indicates information that has changed from previously issued version.

Full text of R-phrases referred to in sections 2 and 3 - Europe : R36/37/38- Irritating to eyes, respiratory system and skin.

Full text of classifications referred to in sections 2 and 3 - Europe : Xi - Irritant

Notice to reader

To the best of our knowledge, the information contained herein is accurate. However, neither the above-named supplier, nor any of its subsidiaries, assumes any liability whatsoever for the accuracy or completeness of the information contained herein.

Final determination of suitability of any material is the sole responsibility of the user. All materials may present unknown hazards and should be used with caution. Although certain hazards are described herein, we cannot guarantee that these are the only hazards that exist.

This product has been classified according to the hazard criteria of the CPR and the MSDS contains all the information required by the CPR.

Material Safety Data Sheet

Thermo
SCIENTIFIC

Immobilized Pepsin

1. Product and company identification

Product name	: Immobilized Pepsin		
Supplier	: Thermo Fisher Scientific Pierce Biotechnology P.O. Box 117 Rockford, IL 61105 United States 815.968.0747 or 800.874.3723	Manufacturer	: Thermo Fisher Scientific Pierce Biotechnology P.O. Box 117 Rockford, IL 61105 United States 815.968.0747 800.874.3723
Product No.	: 0020343 0020343B 1861443 1861457 1880260		
MSDS #	: 103		
Validation date	: 6/2/2008.		
Print date	: 6/2/2008.		
Responsible name	: MSDS (Regulatory Affairs)		
<u>In case of emergency</u>	: CHEMTREC: 800.424.9300 OUTSIDE US: 202.483.7616	<u>Use of Substance/Preparation</u>	: Refer to the instruction booklet for proper and intended use. Otherwise, contact supplier for specific applications.

2. Hazards identification

Physical state	: Liquid. [Gelatinous precipitate.]
OSHA/HCS status	: This material is considered hazardous by the OSHA Hazard Communication Standard (29 CFR 1910.1200).
Emergency overview	: WARNING ! CAUSES RESPIRATORY TRACT, EYE AND SKIN IRRITATION. CONTAINS MATERIAL THAT CAN CAUSE TARGET ORGAN DAMAGE. Irritating to eyes, respiratory system and skin. Avoid exposure - obtain special instructions before use. Do not breathe vapor or mist. Avoid contact with eyes, skin and clothing. Contains material that can cause target organ damage. Use only with adequate ventilation. Keep container tightly closed and sealed until ready for use. Wash thoroughly after handling.
Routes of entry	: Eye contact. Inhalation. Ingestion.
<u>Potential acute health effects</u>	
Inhalation	: Irritating to respiratory system.
Ingestion	: No known significant effects or critical hazards.
Skin	: Irritating to skin.
Eyes	: Irritating to eyes.
<u>Potential chronic health effects</u>	
Chronic effects	: Contains material that can cause target organ damage.
Carcinogenicity	: No known significant effects or critical hazards.
Mutagenicity	: No known significant effects or critical hazards.
Teratogenicity	: No known significant effects or critical hazards.
Developmental effects	: No known significant effects or critical hazards.
Fertility effects	: No known significant effects or critical hazards.
Target organs	: Contains material which causes damage to the following organs: kidneys, bladder. Contains material which may cause damage to the following organs: upper respiratory tract, skin, eye, lens or cornea.

2. Hazards identification

Over-exposure signs/symptoms

Inhalation	: Adverse symptoms may include the following: respiratory tract irritation coughing
Ingestion	: No specific data.
Skin	: Adverse symptoms may include the following: irritation redness
Eyes	: Adverse symptoms may include the following: pain or irritation watering redness
Medical conditions aggravated by over-exposure	: Pre-existing disorders involving any target organs mentioned in this MSDS as being at risk may be aggravated by over-exposure to this product.

The preparation is classified as dangerous according to Directive 1999/45/EC and its amendments.

Classification : Xi; R36/37/38
R42

Human health hazards : Irritating to eyes, respiratory system and skin. May cause sensitization by inhalation.

See toxicological information (section 11)

3. Composition/information on ingredients

United States

<u>Name</u>	<u>CAS number</u>	<u>%</u>
Glycerol	56-81-5	20 - 25
Sodium Acetate	127-09-3	1 - 3

Europe

Substance/preparation : Preparation

<u>Ingredient name</u>	<u>CAS number</u>	<u>%</u>	<u>EC number</u>	<u>Classification</u>
Glycerol	56-81-5	20 - 25	200-289-5	Xi; R36/37/38 [1] [2]
Sodium Acetate	127-09-3	1 - 3	204-823-8	Not classified. [2]
Pepsin	9001-75-6	0.1 - 1	232-629-3	Xi; R36/37/38 R42 [1]

There are no ingredients or additional ingredients present which, within the current knowledge of the supplier and in the concentrations applicable, are classified as hazardous to health or the environment and hence require reporting in this section.

[1] Substance classified with a health or environmental hazard

[2] Substance with a workplace exposure limit

Occupational exposure limits, if available, are listed in section 8.

4 . First aid measures

- Inhalation** : Move exposed person to fresh air. If it is suspected that fumes are still present, the rescuer should wear an appropriate mask or self-contained breathing apparatus. Keep person warm and at rest. If not breathing, if breathing is irregular or if respiratory arrest occurs, provide artificial respiration or oxygen by trained personnel. It may be dangerous to the person providing aid to give mouth-to-mouth resuscitation. Get medical attention. If unconscious, place in recovery position and get medical attention immediately. Maintain an open airway. Loosen tight clothing such as a collar, tie, belt or waistband.
- Ingestion** : Wash out mouth with water. Remove dentures if any. Move exposed person to fresh air. Keep person warm and at rest. If material has been swallowed and the exposed person is conscious, give small quantities of water to drink. Stop if the exposed person feels sick as vomiting may be dangerous. Do not induce vomiting unless directed to do so by medical personnel. If vomiting occurs, the head should be kept low so that vomit does not enter the lungs. Get medical attention. Never give anything by mouth to an unconscious person. If unconscious, place in recovery position and get medical attention immediately. Maintain an open airway. Loosen tight clothing such as a collar, tie, belt or waistband.
- Skin contact** : Flush contaminated skin with plenty of water. Remove contaminated clothing and shoes. Continue to rinse for at least 10 minutes. Get medical attention. Wash clothing before reuse. Clean shoes thoroughly before reuse.
- Eye contact** : Immediately flush eyes with plenty of water for at least 15 minutes, occasionally lifting the upper and lower eyelids. Check for and remove any contact lenses. Get medical attention.
- Protection of first-aiders** : No action shall be taken involving any personal risk or without suitable training. If it is suspected that fumes are still present, the rescuer should wear an appropriate mask or self-contained breathing apparatus. It may be dangerous to the person providing aid to give mouth-to-mouth resuscitation.

See section 11 for more detailed information on health effects and symptoms.

5 . Fire-fighting measures

- Flammability of the product** : In a fire or if heated, a pressure increase will occur and the container may burst.
- Extinguishing media**
- Suitable** : Use an extinguishing agent suitable for the surrounding fire.
- Not suitable** : None known.
- Special exposure hazards** : Promptly isolate the scene by removing all persons from the vicinity of the incident if there is a fire. No action shall be taken involving any personal risk or without suitable training.
- Hazardous combustion products** : Decomposition products may include the following materials:
carbon oxides
metal oxide/oxides
- Special protective equipment for fire-fighters** : Fire-fighters should wear appropriate protective equipment and self-contained breathing apparatus (SCBA) with a full face-piece operated in positive pressure mode.

6 . Accidental release measures

- Personal precautions** : No action shall be taken involving any personal risk or without suitable training. Evacuate surrounding areas. Keep unnecessary and unprotected personnel from entering. Do not touch or walk through spilled material. Avoid breathing vapor or mist. Provide adequate ventilation. Wear appropriate respirator when ventilation is inadequate. Put on appropriate personal protective equipment (see section 8).
- Environmental precautions** : Avoid dispersal of spilled material and runoff and contact with soil, waterways, drains and sewers. Inform the relevant authorities if the product has caused environmental pollution (sewers, waterways, soil or air).

6 . Accidental release measures

- Large spill** : Stop leak if without risk. Move containers from spill area. Approach release from upwind. Prevent entry into sewers, water courses, basements or confined areas. Wash spillages into an effluent treatment plant or proceed as follows. Contain and collect spillage with non-combustible, absorbent material e.g. sand, earth, vermiculite or diatomaceous earth and place in container for disposal according to local regulations (see section 13). Dispose of via a licensed waste disposal contractor. Contaminated absorbent material may pose the same hazard as the spilled product. Note: see section 1 for emergency contact information and section 13 for waste disposal.
- Small spill** : Stop leak if without risk. Move containers from spill area. Dilute with water and mop up if water-soluble or absorb with an inert dry material and place in an appropriate waste disposal container. Dispose of via a licensed waste disposal contractor.

7 . Handling and storage

- Handling** : Put on appropriate personal protective equipment (see section 8). Eating, drinking and smoking should be prohibited in areas where this material is handled, stored and processed. Workers should wash hands and face before eating, drinking and smoking. Do not get in eyes or on skin or clothing. Do not breathe vapor or mist. Do not ingest. Use only with adequate ventilation. Wear appropriate respirator when ventilation is inadequate. Keep in the original container or an approved alternative made from a compatible material, kept tightly closed when not in use. Empty containers retain product residue and can be hazardous. Do not reuse container.
- Storage** : Store between the following temperatures: 2 to 8°C (35.6 to 46.4°F). Store in accordance with local regulations. Store in original container protected from direct sunlight in a dry, cool and well-ventilated area, away from incompatible materials (see section 10) and food and drink. Keep container tightly closed and sealed until ready for use. Containers that have been opened must be carefully resealed and kept upright to prevent leakage. Do not store in unlabeled containers. Use appropriate containment to avoid environmental contamination.

8 . Exposure controls/personal protection

Product name

United States

glycerin

Exposure limits

ACGIH (United States).

TWA: 10 mg/m³

ACGIH TLV (United States).

TWA: 10 mg/m³ 8 hour(s). Form: Total particulates

OSHA PEL (United States).

TWA: 15 mg/m³ 8 hour(s). Form: Total dust

ACGIH TLV (United States, 1/2007).

TWA: 10 mg/m³ 8 hour(s). Form: Mist

OSHA PEL (United States, 11/2006).

TWA: 5 mg/m³ 8 hour(s). Form: Respirable fraction

TWA: 15 mg/m³ 8 hour(s). Form: Total dust

OSHA PEL 1989 (United States, 3/1989).

TWA: 5 mg/m³ 8 hour(s). Form: Respirable fraction

TWA: 10 mg/m³ 8 hour(s). Form: Total dust

ACGIH TLV (United States).

TWA: 10 mg/m³ 8 hour(s). Form: Total particulates

OSHA PEL (United States).

TWA: 15 mg/m³ 8 hour(s). Form: Total dust

OSHA PEL (United States). Notes: Respirable

TWA: 15 mg/m³ 8 hour(s).

acetic acid, sodium salt

OSHA (United States).

PEL: 15 mg/m³ Form: Total dust

PEL: 5 mg/m³ Form: Respirable fraction

ACGIH (United States).

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8 . Exposure controls/personal protection

TLV: 10 mg/m³ Form: Dust Containing no Abestos

Europe

glycerin

ACGIH (United States).

TWA: 10 mg/m³

ACGIH TLV (United States).

TWA: 10 mg/m³ 8 hour(s). Form: Total particulates

TWA: 10 mg/m³ 8 hour(s). Form: Mist

TWA: 10 mg/m³ 8 hour(s). Form: Total particulates

acetic acid, sodium salt

ACGIH (United States).

TLV: 10 mg/m³ Form: Dust Containing no Abestos

Consult local authorities for acceptable exposure limits.

Recommended monitoring procedures : If this product contains ingredients with exposure limits, personal, workplace atmosphere or biological monitoring may be required to determine the effectiveness of the ventilation or other control measures and/or the necessity to use respiratory protective equipment.

Engineering measures : Use only with adequate ventilation. If user operations generate dust, fumes, gas, vapor or mist, use process enclosures, local exhaust ventilation or other engineering controls to keep worker exposure to airborne contaminants below any recommended or statutory limits.

Hygiene measures : Wash hands, forearms and face thoroughly after handling chemical products, before eating, smoking and using the lavatory and at the end of the working period. Appropriate techniques should be used to remove potentially contaminated clothing. Wash contaminated clothing before reusing. Ensure that eyewash stations and safety showers are close to the workstation location.

Personal protection

Respiratory

: Use a properly fitted, air-purifying or air-fed respirator complying with an approved standard if a risk assessment indicates this is necessary. Respirator selection must be based on known or anticipated exposure levels, the hazards of the product and the safe working limits of the selected respirator.

Hands

: Chemical-resistant, impervious gloves complying with an approved standard should be worn at all times when handling chemical products if a risk assessment indicates this is necessary.

Eyes

: Safety eyewear complying with an approved standard should be used when a risk assessment indicates this is necessary to avoid exposure to liquid splashes, mists, gases or dusts.

Skin

: Personal protective equipment for the body should be selected based on the task being performed and the risks involved and should be approved by a specialist before handling this product.

Environmental exposure controls

: Emissions from ventilation or work process equipment should be checked to ensure they comply with the requirements of environmental protection legislation. In some cases, fume scrubbers, filters or engineering modifications to the process equipment will be necessary to reduce emissions to acceptable levels.

9 . Physical and chemical properties

Physical state : Liquid. [Gelatinous precipitate.]

Color : White.

Dispersibility properties : Easily dispersible in the following materials: cold water and hot water.

10 . Stability and reactivity

Chemical stability	: The product is stable. Under normal conditions of storage and use, hazardous polymerization will not occur.
Conditions to avoid	: No specific data.
Incompatible materials	: No specific data.
Hazardous decomposition products	: Under normal conditions of storage and use, hazardous decomposition products should not be produced.
Possibility of hazardous reactions	: Will not occur.

11 . Toxicological information

United States

Acute toxicity

Product/ingredient name	Result	Species	Dose	Exposure
glycerin	LD50 Dermal	Rabbit	>10 g/kg	-
	LD50 Intraperitoneal	Rat	4420 mg/kg	-
	LD50 Intravenous	Rat	5566 mg/kg	-
	LD50 Oral	Rat	12600 mg/kg	-
	LD50 Oral	Rat	12600 mg/kg	-
	LD50 Oral	Mouse	4090 mg/kg	-
	LD50 Subcutaneous	Rat	100 mg/kg	-
	LDLo Intramuscular	Rat	10 mg/kg	-
	TDLo Intramuscular	Rat	8 mL/kg	-
	TDLo Intramuscular	Rat	5000 mg/kg	-
acetic acid, sodium salt	LD50 Dermal	Rabbit	>10 g/kg	-
	LD50 Dermal	Rabbit	>10000 mg/kg	-
	LD50 Oral	Rat	3530 mg/kg	-
	LD50 Oral	Mouse	6891 mg/kg	-
	LD50 Oral	Rat	3530 mg/kg	-

Conclusion/Summary : Not available.

Chronic toxicity

Conclusion/Summary : Not available.

Carcinogenicity

Conclusion/Summary : Not available.

Classification

Product/ingredient name	ACGIH	IARC	EPA	NIOSH	NTP	OSHA
glycerin	-	-	-	-	-	None.
acetic acid, sodium salt	-	-	-	None.	-	None.

Mutagenicity

Conclusion/Summary : Not available.

Teratogenicity

Conclusion/Summary : Not available.

Reproductive toxicity

Conclusion/Summary : Not available.

Europe

Chronic effects : Once sensitized, a severe allergic reaction may occur when subsequently exposed to very low levels.

11 . Toxicological information

- Carcinogenicity** : No known significant effects or critical hazards.
Mutagenicity : No known significant effects or critical hazards.
Teratogenicity : No known significant effects or critical hazards.
Developmental effects : No known significant effects or critical hazards.
Fertility effects : No known significant effects or critical hazards.

12 . Ecological information

- Environmental effects** : No known significant effects or critical hazards.
United States
Aquatic ecotoxicity
Conclusion/Summary : Not available.
Other adverse effects : No known significant effects or critical hazards.

13 . Disposal considerations

- Waste disposal** : The generation of waste should be avoided or minimized wherever possible. Dispose of surplus and non-recyclable products via a licensed waste disposal contractor. Disposal of this product, solutions and any by-products should at all times comply with the requirements of environmental protection and waste disposal legislation and any regional local authority requirements. Avoid dispersal of spilled material and runoff and contact with soil, waterways, drains and sewers.

- Hazardous waste** : The classification of the product may meet the criteria for a hazardous waste.

Disposal should be in accordance with applicable regional, national and local laws and regulations.

Refer to Section 7: HANDLING AND STORAGE and Section 8: EXPOSURE CONTROLS/PERSONAL PROTECTION for additional handling information and protection of employees.

14 . Transport information

Regulatory information	UN number	Proper shipping name	Classes	PG*
DOT Classification	Not regulated.	-	-	-
IATA-DGR Class	Not available.	Not available.	Not available.	-

PG* : Packing group

15 . Regulatory information

United States

- HCS Classification** : Irritating material
Target organ effects
- U.S. Federal regulations** : **United States inventory (TSCA 8b)**: All components are listed or exempted.
SARA 302/304/311/312 extremely hazardous substances: No products were found.
SARA 302/304 emergency planning and notification: No products were found.
SARA 302/304/311/312 hazardous chemicals: glycerin; acetic acid, sodium salt
SARA 311/312 MSDS distribution - chemical inventory - hazard identification:
glycerin: Immediate (acute) health hazard, Delayed (chronic) health hazard; acetic acid, sodium salt: Immediate (acute) health hazard
Clean Water Act (CWA) 307: No products were found.
Clean Water Act (CWA) 311: No products were found.
Clean Air Act (CAA) 112 accidental release prevention: No products were found.

15 . Regulatory information

Clean Air Act (CAA) 112 regulated flammable substances: No products were found.

Clean Air Act (CAA) 112 regulated toxic substances: No products were found.

Canada

WHMIS (Canada)

Canadian lists

- : Class D-2B: Material causing other toxic effects (Toxic).
- : **CEPA Toxic substances:** None of the components are listed.
- Canadian ARET:** None of the components are listed.
- Canadian NPRI:** None of the components are listed.
- Alberta Designated Substances:** None of the components are listed.
- Ontario Designated Substances:** None of the components are listed.
- Quebec Designated Substances:** None of the components are listed.

Canada inventory

- : **Canada inventory:** All components are listed or exempted.

EU regulations

Hazard symbol or symbols



Harmful

Risk phrases

- : R36/37/38- Irritating to eyes, respiratory system and skin.
- R42- May cause sensitization by inhalation.

Safety phrases

- : S23- Do not breathe [***].
- S45- In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).

International regulations

International lists

- : **Australia inventory (AICS):** All components are listed or exempted.
- China inventory (IECSC):** All components are listed or exempted.
- Korea inventory (KECI):** All components are listed or exempted.
- Philippines inventory (PICCS):** All components are listed or exempted.
- Japan inventory (ENCS):** Not determined.

16 . Other information

Label requirements

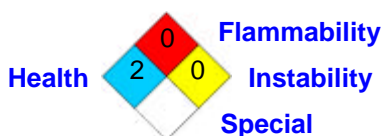
- : CAUSES RESPIRATORY TRACT, EYE AND SKIN IRRITATION. CONTAINS MATERIAL THAT CAN CAUSE TARGET ORGAN DAMAGE.

Hazardous Material Information System (U.S.A.)

Health	2
Flammability	0
Physical hazards	0

The customer is responsible for determining the PPE code for this material.

National Fire Protection Association (U.S.A.)



Date of printing

: 6/2/2008.

Date of issue

: 6/2/2008.

Date of previous issue

: 2/29/2008.

16 . Other information

Version : 1.01

 Indicates information that has changed from previously issued version.

Full text of R-phrases referred to in sections 2 and 3 - Europe : R36/37/38- Irritating to eyes, respiratory system and skin.
R42- May cause sensitization by inhalation.

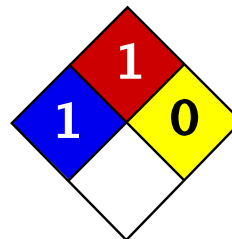
Full text of classifications referred to in sections 2 and 3 - Europe : Xi - Irritant

Notice to reader

To the best of our knowledge, the information contained herein is accurate. However, neither the above-named supplier, nor any of its subsidiaries, assumes any liability whatsoever for the accuracy or completeness of the information contained herein.

Final determination of suitability of any material is the sole responsibility of the user. All materials may present unknown hazards and should be used with caution. Although certain hazards are described herein, we cannot guarantee that these are the only hazards that exist.

This product has been classified according to the hazard criteria of the CPR and the MSDS contains all the information required by the CPR.



Health	1
Fire	1
Reactivity	0
Personal Protection	A

Material Safety Data Sheet L-Glutamine MSDS

Section 1: Chemical Product and Company Identification

Product Name: L-Glutamine

Catalog Codes: SLG1462, SLG1963

CAS#: 56-85-9

RTECS: MA2275100

TSCA: TSCA 8(b) inventory: L-Glutamine

CI#: Not available.

Synonym: L-2-Aminoglutaramic acid

Chemical Formula: C₅H₁₀N₂O₃

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.

Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:

1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
{L-}Glutamine	56-85-9	100

Toxicological Data on Ingredients: L-Glutamine: ORAL (LD50): Acute: 7500 mg/kg [Rat]. 21700 mg/kg [Mouse].

Section 3: Hazards Identification

Potential Acute Health Effects: Hazardous in case of ingestion. Slightly hazardous in case of eye contact (irritant), of inhalation.

Potential Chronic Health Effects:

Hazardous in case of ingestion.

Slightly hazardous in case of eye contact (irritant), of inhalation.

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Not available.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

The substance is toxic to lungs, mucous membranes.

Repeated or prolonged exposure to the substance can produce target organs damage.

Section 4: First Aid Measures

Eye Contact: Immediately flush eyes with running water for at least 15 minutes, keeping eyelids open. Cold water may be used.

Skin Contact: No known effect on skin contact, rinse with water for a few minutes.

Serious Skin Contact: Not available.

Inhalation: Allow the victim to rest in a well ventilated area. Seek immediate medical attention.

Serious Inhalation: Not available.

Ingestion:

Do not induce vomiting. Loosen tight clothing such as a collar, tie, belt or waistband. If the victim is not breathing, perform mouth-to-mouth resuscitation. Seek immediate medical attention.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: May be combustible at high temperature.

Auto-Ignition Temperature: Not available.

Flash Points: Not available.

Flammable Limits: Not available.

Products of Combustion: These products are carbon oxides (CO, CO₂), nitrogen oxides (NO, NO₂...).

Fire Hazards in Presence of Various Substances: Not available.

Explosion Hazards in Presence of Various Substances:

Risks of explosion of the product in presence of mechanical impact: Not available.

Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions:

SMALL FIRE: Use DRY chemical powder.

LARGE FIRE: Use water spray, fog or foam. Do not use water jet.

Special Remarks on Fire Hazards: Not available.

Special Remarks on Explosion Hazards: Not available.

Section 6: Accidental Release Measures

Small Spill:

Use appropriate tools to put the spilled solid in a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:

Use a shovel to put the material into a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and allow to evacuate through the sanitary system.

Section 7: Handling and Storage

Precautions:

Keep away from heat. Keep away from sources of ignition. Empty containers pose a fire risk, evaporate the

residue under a fume hood. Ground all equipment containing material. Do not ingest. Do not breathe dust. If ingested, seek medical advice immediately and show the container or the label.

Storage:

Keep container dry. Keep in a cool place. Ground all equipment containing material. Keep container tightly closed. Keep in a cool, well-ventilated place. Combustible materials should be stored away from extreme heat and away from strong oxidizing agents.

Section 8: Exposure Controls/Personal Protection

Engineering Controls:

Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection: Safety glasses. Lab coat.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Boots. Gloves. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid. (Solid crystalline powder.)

Odor: Not available.

Taste: Not available.

Molecular Weight: 146.15 g/mole

Color: White.

pH (1% soln/water): 7 [Neutral.]

Boiling Point: Not available.

Melting Point: Decomposes. (185°C or 365°F)

Critical Temperature: Not available.

Specific Gravity: Not available.

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility: Soluble in cold water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Not available.

Incompatibility with various substances: Not available.

Corrosivity: Not available.

Special Remarks on Reactivity: Not available.

Special Remarks on Corrosivity: Not available.

Polymerization: No.

Section 11: Toxicological Information

Routes of Entry: Ingestion.

Toxicity to Animals: Acute oral toxicity (LD50): 7500 mg/kg [Rat].

Chronic Effects on Humans: The substance is toxic to lungs, mucous membranes.

Other Toxic Effects on Humans:

Hazardous in case of ingestion.

Slightly hazardous in case of inhalation.

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: Passes through the placental barrier in animal.

Special Remarks on other Toxic Effects on Humans: Nuisance dust.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are more toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: Not applicable.

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations: TSCA 8(b) inventory: L-Glutamine

Other Regulations: OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

Other Classifications:

WHMIS (Canada): CLASS D-2A: Material causing other toxic effects (VERY TOXIC).

DSCL (EEC):

This product is not classified according to the EU regulations.

HMIS (U.S.A.):

Health Hazard: 1

Fire Hazard: 1

Reactivity: 0

Personal Protection: a

National Fire Protection Association (U.S.A.):

Health: 1

Flammability: 1

Reactivity: 0

Specific hazard:

Protective Equipment:

Not applicable.

Lab coat.

Wear appropriate respirator when ventilation is inadequate.

Safety glasses.

Section 16: Other Information

References: Not available.

Other Special Considerations: Not available.

Created: 10/09/2005 05:38 PM

Last Updated: 11/06/2008 12:00 PM

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MATERIAL SAFETY DATA SHEET

Date Printed: 03/30/2009

Date Updated: 01/27/2006

Version 1.7

Section 1 - Product and Company Information

Product Name	EX-CELL(TM) ACF CHO MEDIUM
Product Number	C9098
Brand	SIGMA
Company	Sigma-Aldrich
Address	3050 Spruce Street SAINT LOUIS MO 63103 US
Technical Phone:	800-325-5832
Fax:	800-325-5052
Emergency Phone:	314-776-6555

Section 2 - Composition/Information on Ingredient

Substance Name	CAS #	SARA 313	
EX-CELL ACF CHO MEDIUM	None	No	
Ingredient Name	CAS #	Percent	SARA 313
Information regarding the specific chemical identity of this material is being withheld as a trade secret of the manufacturer.	None		

Section 3 - Hazards Identification

EMERGENCY OVERVIEW

Irritant.

Irritating to eyes, respiratory system and skin.

HMIS RATING

HEALTH: 2

FLAMMABILITY: 0

REACTIVITY: 0

NFPA RATING

HEALTH: 2

FLAMMABILITY: 0

REACTIVITY: 0

For additional information on toxicity, please refer to Section 11.

Section 4 - First Aid Measures

ORAL EXPOSURE

If swallowed, wash out mouth with water provided person is conscious. Call a physician.

INHALATION EXPOSURE

If inhaled, remove to fresh air. If not breathing give artificial respiration. If breathing is difficult, give oxygen.

DERMAL EXPOSURE

In case of contact, immediately wash skin with soap and copious amounts of water.

EYE EXPOSURE

In case of contact, immediately flush eyes with copious amounts of water for at least 15 minutes.

Section 5 - Fire Fighting Measures

FLASH POINT

N/A

AUTOIGNITION TEMP

N/A

FLAMMABILITY

N/A

EXTINGUISHING MEDIA

Suitable: Water spray. Carbon dioxide, dry chemical powder, or appropriate foam.

FIREFIGHTING

Protective Equipment: Wear self-contained breathing apparatus and protective clothing to prevent contact with skin and eyes.
Specific Hazard(s): Emits toxic fumes under fire conditions.

Section 6 - Accidental Release Measures

PROCEDURE(S) OF PERSONAL PRECAUTION(S)

Wear respirator, chemical safety goggles, rubber boots, and heavy rubber gloves.

METHODS FOR CLEANING UP

Sweep up, place in a bag and hold for waste disposal. Avoid raising dust. Ventilate area and wash spill site after material pickup is complete.

Section 7 - Handling and Storage

HANDLING

User Exposure: Do not breathe dust. Avoid contact with eyes, skin, and clothing. Avoid prolonged or repeated exposure.

STORAGE

Suitable: Keep tightly closed.
Store at 2-8°C

Section 8 - Exposure Controls / PPE

ENGINEERING CONTROLS

Safety shower and eye bath. Mechanical exhaust required.

PERSONAL PROTECTIVE EQUIPMENT

Respiratory: Use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU). Where risk assessment shows air-purifying respirators are appropriate use a dust mask type N95 (US) or type P1 (EN 143) respirator.
Hand: Compatible chemical-resistant gloves.
Eye: Chemical safety goggles.

GENERAL HYGIENE MEASURES

Wash thoroughly after handling.

Section 9 - Physical/Chemical Properties

Appearance	Physical State: Solid	
Property	Value	At Temperature or Pressure
Molecular Weight	N/A	
pH	N/A	
BP/BP Range	N/A	
MP/MP Range	N/A	
Freezing Point	N/A	
Vapor Pressure	N/A	
Vapor Density	N/A	
Saturated Vapor Conc.	N/A	
SG/Density	N/A	
Bulk Density	N/A	
Odor Threshold	N/A	
Volatile%	N/A	
VOC Content	N/A	
Water Content	N/A	
Solvent Content	N/A	
Evaporation Rate	N/A	
Viscosity	N/A	
Surface Tension	N/A	
Partition Coefficient	N/A	
Decomposition Temp.	N/A	
Flash Point	N/A	
Explosion Limits	N/A	
Flammability	N/A	
Autoignition Temp	N/A	
Refractive Index	N/A	
Optical Rotation	N/A	
Miscellaneous Data	N/A	
Solubility	N/A	

N/A = not available

Section 10 - Stability and Reactivity

STABILITY

Stable: Stable.

Materials to Avoid: Strong oxidizing agents.

HAZARDOUS DECOMPOSITION PRODUCTS

Hazardous Decomposition Products: Nature of decomposition products not known.

HAZARDOUS POLYMERIZATION

Hazardous Polymerization: Will not occur

Section 11 - Toxicological Information

ROUTE OF EXPOSURE

Skin Contact: Causes skin irritation.

Skin Absorption: May be harmful if absorbed through the skin.

Eye Contact: Causes eye irritation.

Inhalation: May be harmful if inhaled. Material is irritating to mucous membranes and upper respiratory tract.

Ingestion: May be harmful if swallowed.

SIGNS AND SYMPTOMS OF EXPOSURE

To the best of our knowledge, the chemical, physical, and toxicological properties have not been thoroughly investigated.

Section 12 - Ecological Information

No data available.

Section 13 - Disposal Considerations

APPROPRIATE METHOD OF DISPOSAL OF SUBSTANCE OR PREPARATION

Contact a licensed professional waste disposal service to dispose of this material. Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber. Observe all federal, state, and local environmental regulations.

Section 14 - Transport Information

DOT

Proper Shipping Name: None
Non-Hazardous for Transport: This substance is considered to be non-hazardous for transport.

IATA

Non-Hazardous for Air Transport: Non-hazardous for air transport.

Section 15 - Regulatory Information

EU ADDITIONAL CLASSIFICATION

Symbol of Danger: Xi
Indication of Danger: Irritant.
R: 36/37/38
Risk Statements: Irritating to eyes, respiratory system and skin.
S: 26-36
Safety Statements: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. Wear suitable protective clothing.

US CLASSIFICATION AND LABEL TEXT

Indication of Danger: Irritant.
Risk Statements: Irritating to eyes, respiratory system and skin.
Safety Statements: After contact with skin, wash immediately with plenty of water. Wear suitable protective clothing.

UNITED STATES REGULATORY INFORMATION

SARA LISTED: No

CANADA REGULATORY INFORMATION

WHMIS Classification: This product has been classified in accordance with the hazard criteria of the CPR, and the MSDS contains all the information required by the CPR.
DSL: No
NDSL: No

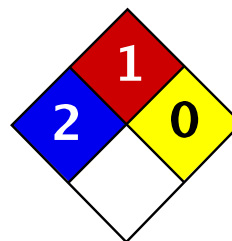
Section 16 - Other Information

DISCLAIMER

For Research or For Further Manufacturing Use

WARRANTY

The above information is believed to be correct but does not purport to be all inclusive and shall be used only as a guide. The information in this document is based on the present state of our knowledge and is applicable to the product with regard to appropriate safety precautions. It does not represent any guarantee of the properties of the product. Sigma-Aldrich Inc., shall not be held liable for any damage resulting from handling or from contact with the above product. See reverse side of invoice or packing slip for additional terms and conditions of sale. Copyright 2009 Sigma-Aldrich Co. License granted to make unlimited paper copies for internal use only.



Health	2
Fire	1
Reactivity	0
Personal Protection	E

Material Safety Data Sheet

MES MSDS

Section 1: Chemical Product and Company Identification

Product Name: MES

Catalog Codes: SLM3343, SLM1198

CAS#: 4432-31-9

RTECS: KI7970000

TSCA: TSCA 8(b) inventory: MES

CI#: Not available.

Synonym: 2-(N-Morpholino)ethanesulfonic acid

Chemical Name: Not available.

Chemical Formula: C6H13NO4S.H2O

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.

Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:

1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
MES	4432-31-9	100

Toxicological Data on Ingredients: MES LD50: Not available. LC50: Not available.

Section 3: Hazards Identification

Potential Acute Health Effects: Very hazardous in case of ingestion. Hazardous in case of skin contact (irritant), of eye contact (irritant).

Potential Chronic Health Effects:

Hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation.

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Not available.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

The substance is toxic to lungs, mucous membranes.

Repeated or prolonged exposure to the substance can produce target organs damage.

Section 4: First Aid Measures

Eye Contact: Check for and remove any contact lenses. Do not use an eye ointment. Seek medical attention.

Skin Contact:

After contact with skin, wash immediately with plenty of water. Gently and thoroughly wash the contaminated skin with running water and non-abrasive soap. Be particularly careful to clean folds, crevices, creases and groin. Cover the irritated skin with an emollient. If irritation persists, seek medical attention. Wash contaminated clothing before reusing.

Serious Skin Contact:

Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek medical attention.

Inhalation: Allow the victim to rest in a well ventilated area. Seek immediate medical attention.

Serious Inhalation: Not available.

Ingestion:

Do not induce vomiting. Loosen tight clothing such as a collar, tie, belt or waistband. If the victim is not breathing, perform mouth-to-mouth resuscitation. Seek immediate medical attention.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: May be combustible at high temperature.

Auto-Ignition Temperature: Not available.

Flash Points: Not available.

Flammable Limits: Not available.

Products of Combustion: These products are carbon oxides (CO, CO₂), nitrogen oxides (NO, NO₂...), sulfur oxides (SO₂, SO₃...).

Fire Hazards in Presence of Various Substances: Not available.

Explosion Hazards in Presence of Various Substances:

Risks of explosion of the product in presence of mechanical impact: Not available.

Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions:

SMALL FIRE: Use DRY chemical powder.

LARGE FIRE: Use water spray, fog or foam. Do not use water jet.

Special Remarks on Fire Hazards: Not available.

Special Remarks on Explosion Hazards: Not available.

Section 6: Accidental Release Measures

Small Spill:

Use appropriate tools to put the spilled solid in a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:

Use a shovel to put the material into a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and allow to evacuate through the sanitary system.

Section 7: Handling and Storage

Precautions:

Keep away from heat. Keep away from sources of ignition. Empty containers pose a fire risk, evaporate the residue under a fume hood. Ground all equipment containing material. Do not breathe dust. Wear suitable protective clothing. If you feel unwell, seek medical attention and show the label when possible. Avoid contact with skin and eyes.

Storage:

Keep container dry. Keep in a cool place. Ground all equipment containing material. Keep container tightly closed. Keep in a cool, well-ventilated place. Combustible materials should be stored away from extreme heat and away from strong oxidizing agents.

Section 8: Exposure Controls/Personal Protection

Engineering Controls:

Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection:

Splash goggles. Lab coat. Dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid. (Powdered solid.)

Odor: Not available.

Taste: Not available.

Molecular Weight: 213.26 g/mole

Color: Colorless.

pH (1% soln/water): Not available.

Boiling Point: Not available.

Melting Point: Not available.

Critical Temperature: Not available.

Specific Gravity: Not available.

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: Not available.

Solubility: Not available.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Not available.

Incompatibility with various substances: Not available.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity: Not available.

Special Remarks on Corrosivity: Not available.

Polymerization: No.

Section 11: Toxicological Information

Routes of Entry: Eye contact. Ingestion.

Toxicity to Animals:

LD50: Not available.

LC50: Not available.

Chronic Effects on Humans: The substance is toxic to lungs, mucous membranes.

Other Toxic Effects on Humans:

Very hazardous in case of ingestion.

Hazardous in case of skin contact (irritant).

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: Not available.

Special Remarks on other Toxic Effects on Humans: Not available.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are more toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: Not applicable.

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations: TSCA 8(b) inventory: MES

Other Regulations: OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

Other Classifications:

WHMIS (Canada): CLASS D-2A: Material causing other toxic effects (VERY TOXIC).

DSCL (EEC): R36/38- Irritating to eyes and skin.

HMIS (U.S.A.):

Health Hazard: 2

Fire Hazard: 1

Reactivity: 0

Personal Protection: E

National Fire Protection Association (U.S.A.):

Health: 2

Flammability: 1

Reactivity: 0

Specific hazard:

Protective Equipment:

Gloves.

Lab coat.

Dust respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate.

Splash goggles.

Section 16: Other Information

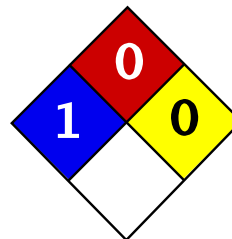
References: Not available.

Other Special Considerations: Not available.

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Last Updated: 11/06/2008 12:00 PM

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Health	1
Fire	0
Reactivity	0
Personal Protection	E

Material Safety Data Sheet

Sodium chloride MSDS

Section 1: Chemical Product and Company Identification

Product Name: Sodium chloride

Catalog Codes: SLS3262, SLS1045, SLS3889, SLS1669, SLS3091

CAS#: 7647-14-5

RTECS: VZ4725000

TSCA: TSCA 8(b) inventory: Sodium chloride

CI#: Not applicable.

Synonym: Salt; Sea Salt

Chemical Name: Sodium chloride

Chemical Formula: NaCl

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.
Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Sodium chloride	7647-14-5	100

Toxicological Data on Ingredients: Sodium chloride: ORAL (LD50): Acute: 3000 mg/kg [Rat]. 4000 mg/kg [Mouse]. DERMAL (LD50): Acute: >10000 mg/kg [Rabbit]. DUST (LC50): Acute: >42000 mg/m 1 hours [Rat].

Section 3: Hazards Identification

Potential Acute Health Effects: Slightly hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation.

Potential Chronic Health Effects:

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells. Mutagenic for bacteria and/or yeast.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

Repeated or prolonged exposure is not known to aggravate medical condition.

Section 4: First Aid Measures

Eye Contact:

Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention.

Skin Contact:

Wash with soap and water. Cover the irritated skin with an emollient. Get medical attention if irritation develops. Cold water may be used.

Serious Skin Contact: Not available.

Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention if symptoms appear.

Serious Inhalation: Not available.

Ingestion:

Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. Loosen tight clothing such as a collar, tie, belt or waistband. Get medical attention if symptoms appear.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: Non-flammable.

Auto-Ignition Temperature: Not applicable.

Flash Points: Not applicable.

Flammable Limits: Not applicable.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances: Not applicable.

Explosion Hazards in Presence of Various Substances:

Risks of explosion of the product in presence of mechanical impact: Not available.

Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions: Not applicable.

Special Remarks on Fire Hazards: When heated to decomposition it emits toxic fumes.

Special Remarks on Explosion Hazards:

Electrolysis of sodium chloride in presence of nitrogenous compounds to produce chlorine may lead to formation of explosive nitrogen trichloride.

Potentially explosive reaction with dichloromaleic anhydride + urea.

Section 6: Accidental Release Measures

Small Spill:

Use appropriate tools to put the spilled solid in a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:

Use a shovel to put the material into a convenient waste disposal container. Finish cleaning by spreading water

on the contaminated surface and allow to evacuate through the sanitary system.

Section 7: Handling and Storage

Precautions:

Keep locked up.. Do not ingest. Do not breathe dust. Avoid contact with eyes. Wear suitable protective clothing. If ingested, seek medical advice immediately and show the container or the label. Keep away from incompatibles such as oxidizing agents, acids.

Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area. Hygroscopic

Section 8: Exposure Controls/Personal Protection

Engineering Controls:

Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection:

Splash goggles. Lab coat. Dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid. (Solid crystalline powder.)

Odor: Slight.

Taste: Saline.

Molecular Weight: 58.44 g/mole

Color: White.

pH (1% soln/water): 7 [Neutral.]

Boiling Point: 1413°C (2575.4°F)

Melting Point: 801°C (1473.8°F)

Critical Temperature: Not available.

Specific Gravity: 2.165 (Water = 1)

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility:

Easily soluble in cold water, hot water.

Soluble in glycerol, and ammonia.

Very slightly soluble in alcohol.

Insoluble in Hydrochloric Acid.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Incompatible materials, high temperatures.

Incompatibility with various substances: Reactive with oxidizing agents, metals, acids.

Corrosivity: Not considered to be corrosive for metals and glass.

Special Remarks on Reactivity:

Hygroscopic.

Reacts with most nonnoble metals such as iron or steel, building materials (such as cement)

Sodium chloride is rapidly attacked by bromine trifluoride.

Violent reaction with lithium.

Special Remarks on Corrosivity: Not available.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Inhalation. Ingestion.

Toxicity to Animals:

WARNING: THE LC50 VALUES HEREUNDER ARE ESTIMATED ON THE BASIS OF A 4-HOUR EXPOSURE.

Acute oral toxicity (LD50): 3000 mg/kg [Rat].

Acute dermal toxicity (LD50): >10000 mg/kg [Rabbit].

Acute toxicity of the dust (LC50): >42000 mg/m³ 1 hours [Rat].

Chronic Effects on Humans: MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells. Mutagenic for bacteria and/or yeast.

Other Toxic Effects on Humans: Slightly hazardous in case of skin contact (irritant), of ingestion, of inhalation.

Special Remarks on Toxicity to Animals: Lowest Published Lethal Dose (LDL) [Man] - Route: Oral; Dose: 1000 mg/kg

Special Remarks on Chronic Effects on Humans:

Causes adverse reproductive effects in humans (fetotoxicity, abortion,) by intraplacental route.

High intake of sodium chloride, whether from occupational exposure or in the diet, may increase risk of TOXEMIA OF PREGNANCY in susceptible women (Bishop, 1978). Hypertonic sodium chloride solutions have been used to induce abortion in late pregnancy by direct infusion into the uterus (Brown et al, 1972), but this route of administration is not relevant to occupational exposures.

May cause adverse reproductive effects and birth defects in animals, particularly rats and mice (fetotoxicity, abortion, musculoskeletal abnormalities, and maternal effects (effects on ovaries, fallopian tubes) by oral,

intraperitoneal, intraplacental, intrauterine, parenteral, and subcutaneous routes. While sodium chloride has been used as a negative control in some reproductive studies, it has also been used as an example that almost any chemical can cause birth defects in experimental animals if studied under the right conditions (Nishimura & Miyamoto, 1969). In experimental animals, sodium chloride has caused delayed effects on newborns, has been fetotoxic, and has caused birth defects and abortions in rats and mice (RTECS, 1997).
May affect genetic material (mutagenic)

Special Remarks on other Toxic Effects on Humans:

Acute Potential Health Effects:

Skin: May cause skin irritation.

Eyes: Causes eye irritation.

Ingestion: Ingestion of large quantities can irritate the stomach (as in overuse of salt tablets) with nausea and vomiting. May affect behavior (muscle spasticity/contraction, somnolence), sense organs, metabolism, and cardiovascular system. Continued exposure may produce dehydration, internal organ congestion, and coma.

Inhalation: Material is irritating to mucous membranes and upper respiratory tract.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The product itself and its products of degradation are not toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: Not applicable.

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations: TSCA 8(b) inventory: Sodium chloride

Other Regulations: EINECS: This product is on the European Inventory of Existing Commercial Chemical Substances.

Other Classifications:

WHMIS (Canada): Not controlled under WHMIS (Canada).

DSCL (EEC):

R40- Possible risks of irreversible effects.

S24/25- Avoid contact with skin and eyes.

HMIS (U.S.A.):

Health Hazard: 1

Fire Hazard: 0

Reactivity: 0

Personal Protection: E

National Fire Protection Association (U.S.A.):

Health: 1

Flammability: 0

Reactivity: 0

Specific hazard:

Protective Equipment:

Gloves.

Lab coat.

Dust respirator. Be sure to use an approved/certified respirator or equivalent.

Splash goggles.

Section 16: Other Information

References:

- Hawley, G.G.. The Condensed Chemical Dictionary, 11e ed., New York N.Y., Van Nostrand Reinold, 1987.
- SAX, N.I. Dangerous Properties of Industrial Materials. Toronto, Van Nostrand Reinold, 6e ed. 1984.
- The Sigma-Aldrich Library of Chemical Safety Data, Edition II.

Other Special Considerations: Not available.

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Last Updated: 11/06/2008 12:00 PM

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Material Safety Data Sheet

PBS Phosphate Buffered Saline

ACC# 89342

Section 1 - Chemical Product and Company Identification

MSDS Name: PBS Phosphate Buffered Saline**Catalog Numbers:** BP661-10, BP661-50, BP665-1**Synonyms:** None.**Company Identification:**

Fisher Scientific

1 Reagent Lane

Fair Lawn, NJ 07410

For information, call: 201-796-7100**Emergency Number:** 201-796-7100**For CHEMTREC assistance, call:** 800-424-9300**For International CHEMTREC assistance, call:** 703-527-3887

Section 2 - Composition, Information on Ingredients

CAS#	Chemical Name	Percent	EINECS/ELINCS
7647-14-5	Sodium Chloride	81.0	231-598-3
7558-79-4	Sodium phosphate, dibasic	~14	231-448-7
7778-77-0	Potassium phosphate, Monobasic	~3.0	231-913-4
7447-40-7	Potassium chloride	~2.0	231-211-8

Section 3 - Hazards Identification

EMERGENCY OVERVIEW

Appearance: white solid.

Warning! Causes eye irritation. May cause skin and respiratory tract irritation.**Target Organs:** Eyes.

Potential Health Effects

Eye: Causes eye irritation.**Skin:** May cause skin irritation.**Ingestion:** Ingestion of large amounts may cause gastrointestinal irritation. May cause gastric disturbances and electrolytic imbalance. Ingestion of large amounts of sodium chloride may cause nausea, and vomiting, rigidity or convulsions. Continued exposure can produce coma, dehydration and internal organ congestion.**Inhalation:** Inhalation of dust may cause respiratory tract irritation.**Chronic:** No information found.

Section 4 - First Aid Measures

Eyes: Flush eyes with plenty of water for at least 15 minutes, occasionally lifting the upper and lower eyelids. Get medical aid.

Skin: Flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Get medical aid if irritation develops or persists. Wash clothing before reuse.

Ingestion: Do not induce vomiting. If victim is conscious and alert, give 2-4 cupfuls of milk or water. Never give anything by mouth to an unconscious person. Get medical aid.

Inhalation: Remove from exposure and move to fresh air immediately. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical aid.

Notes to Physician: Treat symptomatically and supportively.

Section 5 - Fire Fighting Measures

General Information: As in any fire, wear a self-contained breathing apparatus in pressure-demand, MSHA/NIOSH (approved or equivalent), and full protective gear. During a fire, irritating and highly toxic gases may be generated by thermal decomposition or combustion. Substance is noncombustible.

Extinguishing Media: Use water spray, dry chemical, carbon dioxide, or chemical foam.

Flash Point: Not applicable.

Autoignition Temperature: Not applicable.

Explosion Limits, Lower: Not available.

Upper: Not available.

NFPA Rating: (estimated) Health: 2; Flammability: 0; Instability: 0

Section 6 - Accidental Release Measures

General Information: Use proper personal protective equipment as indicated in Section 8.

Spills/Leaks: Vacuum or sweep up material and place into a suitable disposal container. Clean up spills immediately, observing precautions in the Protective Equipment section. Avoid generating dusty conditions. Provide ventilation.

Section 7 - Handling and Storage

Handling: Wash thoroughly after handling. Use with adequate ventilation. Avoid contact with eyes, skin, and clothing. Avoid ingestion and inhalation.

Storage: Store in a tightly closed container. Store in a cool, dry, well-ventilated area away from incompatible substances.

Section 8 - Exposure Controls, Personal Protection

Engineering Controls: Facilities storing or utilizing this material should be equipped with an eyewash

facility and a safety shower. Use adequate ventilation to keep airborne concentrations low.

Exposure Limits

Chemical Name	ACGIH	NIOSH	OSHA - Final PELs
Sodium Chloride	none listed	none listed	none listed
Sodium phosphate, dibasic	none listed	none listed	none listed
Potassium phosphate, Monobasic	none listed	none listed	none listed
Potassium chloride	none listed	none listed	none listed

OSHA Vacated PELs: Sodium Chloride: No OSHA Vacated PELs are listed for this chemical. Sodium phosphate, dibasic: No OSHA Vacated PELs are listed for this chemical. Potassium phosphate, Monobasic: No OSHA Vacated PELs are listed for this chemical. Potassium chloride: No OSHA Vacated PELs are listed for this chemical.

Personal Protective Equipment

Eyes: Wear appropriate protective eyeglasses or chemical safety goggles as described by OSHA's eye and face protection regulations in 29 CFR 1910.133 or European Standard EN166.

Skin: Wear appropriate protective gloves to prevent skin exposure.

Clothing: Wear appropriate protective clothing to prevent skin exposure.

Respirators: Follow the OSHA respirator regulations found in 29 CFR 1910.134 or European Standard EN 149. Use a NIOSH/MSHA or European Standard EN 149 approved respirator if exposure limits are exceeded or if irritation or other symptoms are experienced.

Section 9 - Physical and Chemical Properties

Physical State: Solid

Appearance: white

Odor: none reported

pH: Not available.

Vapor Pressure: Not available.

Vapor Density: Not available.

Evaporation Rate: Not available.

Viscosity: Not available.

Boiling Point: Not available.

Freezing/Melting Point: Not available.

Decomposition Temperature: Not available.

Solubility: Soluble.

Specific Gravity/Density: Not available.

Molecular Formula: Mixture

Molecular Weight: Not available.

Section 10 - Stability and Reactivity

Chemical Stability: Stable.

Conditions to Avoid: Dust generation, excess heat.

Incompatibilities with Other Materials: Potassium chloride is incompatible with potassium permanganate. Sodium chloride is incompatible with dichloromaleic anhydride + urea, lithium, and nitrogen compounds. Potassium phosphate dibasic and monobasic may react violently with strong acids.

Hazardous Decomposition Products: Oxides of phosphorus, sodium oxide, oxides of potassium.

Hazardous Polymerization: Will not occur.

Section 11 - Toxicological Information

RTECS#:

CAS# 7647-14-5: VZ4725000

CAS# 7558-79-4: WC4500000

CAS# 7778-77-0: TC6615500

CAS# 7447-40-7: TS8050000

LD50/LC50:

CAS# 7647-14-5:

Draize test, rabbit, eye: 100 mg Mild;

Draize test, rabbit, eye: 100 mg/24H Moderate;

Draize test, rabbit, eye: 10 mg Moderate;

Draize test, rabbit, skin: 50 mg/24H Mild;

Draize test, rabbit, skin: 500 mg/24H Mild;

Inhalation, rat: LC50 = >42 gm/m³/1H;

Oral, mouse: LD50 = 4 gm/kg;

Oral, rat: LD50 = 3000 mg/kg;

Skin, rabbit: LD50 = >10 gm/kg;

CAS# 7558-79-4:

Draize test, rabbit, eye: 500 mg/24H Mild;

Draize test, rabbit, skin: 500 mg/24H Mild;

Oral, rat: LD50 = 17 gm/kg;

CAS# 7778-77-0:

Skin, rabbit: LD50 = >4640 mg/kg;

CAS# 7447-40-7:

Draize test, rabbit, eye: 500 mg/24H Mild;

Oral, mouse: LD50 = 1500 mg/kg;

Oral, rat: LD50 = 2600 mg/kg;

Carcinogenicity:

CAS# 7647-14-5: Not listed by ACGIH, IARC, NTP, or CA Prop 65.

CAS# 7558-79-4: Not listed by ACGIH, IARC, NTP, or CA Prop 65.

CAS# 7778-77-0: Not listed by ACGIH, IARC, NTP, or CA Prop 65.

CAS# 7447-40-7: Not listed by ACGIH, IARC, NTP, or CA Prop 65.

Epidemiology: No information found.

Teratogenicity: No information found.

Reproductive Effects: No information found.

Mutagenicity: No information found.

Neurotoxicity: No information found.

Other Studies:

Section 12 - Ecological Information

No information available.

Section 13 - Disposal Considerations

Chemical waste generators must determine whether a discarded chemical is classified as a hazardous waste. US EPA guidelines for the classification determination are listed in 40 CFR Parts 261.3. Additionally, waste generators must consult state and local hazardous waste regulations to ensure complete and accurate classification.

RCRA P-Series: None listed.

RCRA U-Series: None listed.

Section 14 - Transport Information

	US DOT	Canada TDG
Shipping Name:	Not regulated as a hazardous material	No information available.
Hazard Class:		
UN Number:		
Packing Group:		

Section 15 - Regulatory Information

US FEDERAL

TSCA

CAS# 7647-14-5 is listed on the TSCA inventory.

CAS# 7558-79-4 is listed on the TSCA inventory.

CAS# 7778-77-0 is listed on the TSCA inventory.

CAS# 7447-40-7 is listed on the TSCA inventory.

Health & Safety Reporting List

None of the chemicals are on the Health & Safety Reporting List.

Chemical Test Rules

None of the chemicals in this product are under a Chemical Test Rule.

Section 12b

None of the chemicals are listed under TSCA Section 12b.

TSCA Significant New Use Rule

None of the chemicals in this material have a SNUR under TSCA.

CERCLA Hazardous Substances and corresponding RQs

CAS# 7558-79-4: 5000 lb final RQ; 2270 kg final RQ

SARA Section 302 Extremely Hazardous Substances

None of the chemicals in this product have a TPQ.

SARA Codes

CAS # 7647-14-5: acute.

CAS # 7778-77-0: acute.

CAS # 7447-40-7: acute.

Section 313

This material contains Potassium phosphate, Monobasic (listed as Water Dissociable Nitrate Compounds), ~3.0%, (CAS# 7778-77-0) which is subject to the reporting requirements of Section 313 of SARA Title III and 40 CFR

This material contains Potassium chloride (listed as Water Dissociable Nitrate Compounds), ~2.0%,

(CAS# 7447-40-7) which is subject to the reporting requirements of Section 313 of SARA Title III and 40 CFR Part 373.

Clean Air Act:

This material does not contain any hazardous air pollutants.

This material does not contain any Class 1 Ozone depleters.

This material does not contain any Class 2 Ozone depleters.

Clean Water Act:

CAS# 7558-79-4 is listed as a Hazardous Substance under the CWA.

None of the chemicals in this product are listed as Priority Pollutants under the CWA.

None of the chemicals in this product are listed as Toxic Pollutants under the CWA.

OSHA:

None of the chemicals in this product are considered highly hazardous by OSHA.

STATE

CAS# 7647-14-5 is not present on state lists from CA, PA, MN, MA, FL, or NJ.

CAS# 7558-79-4 can be found on the following state right to know lists: California, New Jersey, Pennsylvania, Massachusetts.

CAS# 7778-77-0 is not present on state lists from CA, PA, MN, MA, FL, or NJ.

CAS# 7447-40-7 is not present on state lists from CA, PA, MN, MA, FL, or NJ.

California Prop 65

California No Significant Risk Level: None of the chemicals in this product are listed.

European/International Regulations**European Labeling in Accordance with EC Directives****Hazard Symbols:**

Not available.

Risk Phrases:**Safety Phrases:****WGK (Water Danger/Protection)**

CAS# 7647-14-5: 0

CAS# 7558-79-4: 1

CAS# 7778-77-0: 1

CAS# 7447-40-7: 1

Canada - DSL/NDSL

CAS# 7647-14-5 is listed on Canada's DSL List.

CAS# 7558-79-4 is listed on Canada's DSL List.

CAS# 7778-77-0 is listed on Canada's DSL List.

CAS# 7447-40-7 is listed on Canada's DSL List.

Canada - WHMIS

This product has a WHMIS classification of D2B.

Canadian Ingredient Disclosure List

CAS# 7778-77-0 is not listed on the Canadian Ingredient Disclosure List.

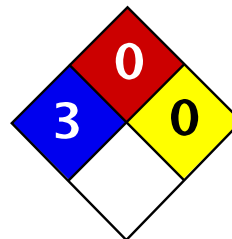
CAS# 7447-40-7 is not listed on the Canadian Ingredient Disclosure List.

Section 16 - Additional Information
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MSDS Creation Date: 7/16/1999

Revision #3 Date: 3/05/2003

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Health	3
Fire	0
Reactivity	0
Personal Protection	

Material Safety Data Sheet

Phosphoric acid, 85% MSDS

Section 1: Chemical Product and Company Identification

Product Name: Phosphoric acid, 85%

Catalog Codes: SLP5569, SLP4555, SLP1732

CAS#: Mixture.

RTECS: Not applicable.

TSCA: TSCA 8(b) inventory: Phosphoric Acid; Water

CI#: Not available.

Synonym: Phosphoric Acid 85%; Phosphoric Acid; Orthophosphoric acid

Chemical Name: Not applicable.

Chemical Formula: Not applicable.

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.

Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Phosphoric Acid	7664-38-2	85-88
Water	7732-18-5	12-15

Toxicological Data on Ingredients: Phosphoric Acid: ORAL (LD50): Acute: 1530 mg/kg [Rat]. DERMAL (LD50): Acute: 2740 mg/kg [Rabbit]. DUST (LC50): Acute: >850 mg/m 1 hours [Rat].

Section 3: Hazards Identification

Potential Acute Health Effects:

Very hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, . Hazardous in case of skin contact (corrosive, permeator), of eye contact (corrosive). Slightly hazardous in case of inhalation (lung sensitizer). Liquid or spray mist may produce tissue damage particularly on mucous membranes of eyes, mouth and respiratory tract. Skin contact may produce burns. Inhalation of the spray mist may produce severe irritation of respiratory tract, characterized by coughing, choking, or shortness of breath. Severe over-exposure can result in death. Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering.

Potential Chronic Health Effects:

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Not available.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

The substance may be toxic to blood, liver, skin, eyes, bone marrow.

Repeated or prolonged exposure to the substance can produce target organs damage. Repeated or prolonged contact with spray mist may produce chronic eye irritation and severe skin irritation. Repeated or prolonged exposure to spray mist may produce respiratory tract irritation leading to frequent attacks of bronchial infection. Repeated exposure to a highly toxic material may produce general deterioration of health by an accumulation in one or many human organs.

Section 4: First Aid Measures

Eye Contact:

Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention immediately.

Skin Contact:

In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Cover the irritated skin with an emollient. Cold water may be used. Wash clothing before reuse. Thoroughly clean shoes before reuse. Get medical attention immediately.

Serious Skin Contact:

Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek immediate medical attention.

Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.

Serious Inhalation:

Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. If breathing is difficult, administer oxygen. If the victim is not breathing, perform mouth-to-mouth resuscitation. WARNING: It may be hazardous to the person providing aid to give mouth-to-mouth resuscitation when the inhaled material is toxic, infectious or corrosive. Seek immediate medical attention.

Ingestion:

Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. If large quantities of this material are swallowed, call a physician immediately. Loosen tight clothing such as a collar, tie, belt or waistband.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: Non-flammable.

Auto-Ignition Temperature: Not applicable.

Flash Points: Not applicable.

Flammable Limits: Not applicable.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances: of metals

Explosion Hazards in Presence of Various Substances: Non-explosive in presence of open flames and sparks, of shocks.

Fire Fighting Media and Instructions: Not applicable.

Special Remarks on Fire Hazards:

Reacts with metals to liberate flammable hydrogen gas.

Formation of flammable gases with aldehydes, cyanides, mercaptins, and sulfides.

Special Remarks on Explosion Hazards: Mixtures with nitromethane are explosive. (Phosphoric Acid)

Section 6: Accidental Release Measures**Small Spill:**

Dilute with water and mop up, or absorb with an inert dry material and place in an appropriate waste disposal container. If necessary: Neutralize the residue with a dilute solution of sodium carbonate.

Large Spill:

Corrosive liquid. Poisonous liquid.

Stop leak if without risk. Absorb with DRY earth, sand or other non-combustible material. Do not get water inside container. Do not touch spilled material. Use water spray curtain to divert vapor drift. Use water spray to reduce vapors. Prevent entry into sewers, basements or confined areas; dike if needed. Call for assistance on disposal. Neutralize the residue with a dilute solution of sodium carbonate. Be careful that the product is not present at a concentration level above TLV. Check TLV on the MSDS and with local authorities.

Section 7: Handling and Storage**Precautions:**

Do not ingest. Do not breathe gas/fumes/ vapor/spray. Never add water to this product. In case of insufficient ventilation, wear suitable respiratory equipment. If ingested, seek medical advice immediately and show the container or the label. Avoid contact with skin and eyes. Keep away from incompatibles such as oxidizing agents, combustible materials, metals, alkalis.

May corrode metallic surfaces. Store in a metallic or coated fiberboard drum using a strong polyethylene inner package.

Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area.

Section 8: Exposure Controls/Personal Protection**Engineering Controls:**

Provide exhaust ventilation or other engineering controls to keep the airborne concentrations of vapors below their respective threshold limit value. Ensure that eyewash stations and safety showers are proximal to the work-station location.

Personal Protection:

Face shield. Full suit. Vapor respirator. Be sure to use an approved/certified respirator or equivalent. Gloves. Boots.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Vapor respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits:

Phosphoric Acid

TWA: 1 STEL: 3 (mg/m³) from ACGIH (TLV) [United States]

TWA: 1 STEL: 3 (mg/m³) from OSHA (PEL) [United States]

TWA: 1 STEL: 3 (mg/m³) from NIOSH

TWA: 1 STEL: 3 (mg/m³) [Mexico] Consult local authorities for acceptable exposure limits.

Section 9: Physical and Chemical Properties

Physical state and appearance: Liquid. (Syrupy liquid Viscous liquid.)

Odor: Odorless.

Taste: Acid.

Molecular Weight: Not applicable.

Color: Clear Colorless.

pH (1% soln/water): Acidic.

Boiling Point: 158°C (316.4°F)

Melting Point: 21°C (69.8°F)

Critical Temperature: Not available.

Specific Gravity: 1.685 @ 25 C (Water = 1)

Vapor Pressure: 0.3 kPa (@ 20°C)

Vapor Density: 3.4 (Air = 1)

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility:

Easily soluble in hot water.

Soluble in cold water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Incompatible materials

Incompatibility with various substances: Reactive with oxidizing agents, combustible materials, metals, alkalis.

Corrosivity:

Extremely corrosive in presence of copper, of stainless steel(304), of stainless steel(316).

Highly corrosive in presence of aluminum.

Non-corrosive in presence of glass.

Special Remarks on Reactivity:

Reacts with metals to liberate flammable hydrogen gas.

Incompatible with sodium tetrahydroborate producing a violent exothermic reaction.

Heat generated with: alcohols, glycols, aldehydes, amides, amines, azo-compounds, carbamates, caustics, esters, ketones, phenols and cresols, organophosphates, epoxides, combustible materials, unsaturated halides, organic peroxides.

Formation of flammable gases, with aldehydes, cyanides, mercaptins, and sulfides.

Formation of toxic fumes with cyanides, fluorides, halogenated organics, sulfides, and organic peroxides.
Do not mix with solutions containing bleach or ammonia.
Incompatible with nitromethane, chlorides + stainless steel.
(Phosphoric Acid)

Special Remarks on Corrosivity:

Minor corrosive effect on bronze.
Severe corrosive effect on brass.
Corrosive to ferrous metals and alloys.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Absorbed through skin. Dermal contact. Eye contact. Inhalation. Ingestion.

Toxicity to Animals:

Acute oral toxicity (LD50): 1530 mg/kg [Rat].
Acute dermal toxicity (LD50): 2740 mg/kg [Rabbit].

Chronic Effects on Humans: May cause damage to the following organs: blood, liver, skin, eyes, bone marrow.

Other Toxic Effects on Humans:

Extremely hazardous in case of inhalation (lung corrosive).
Very hazardous in case of skin contact (irritant), of ingestion, .
Hazardous in case of skin contact (corrosive, permeator), of eye contact (corrosive).

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: Not available.

Special Remarks on other Toxic Effects on Humans:

Acute Potential Health Effects:
Skin: Corrosive and causes severe skin irritation and can cause severe skin burns. May affect behavior (somnolence or excitement) if absorbed through skin.
Eyes: Corrosive. Liquid or vapor causes severe eye irritation and can cause severe eye burns leading to permanent corneal damage or chemical conjunctivitis.
Ingestion: May be harmful if swallowed. Causes irritation and burns of the gastrointestinal (digestive) tract. Causes severe pain, nausea, vomiting, diarrhea hematemesis, gastrointestinal hemorrhaging, and shock. May cause corrosion and permanent tissue destruction of the esophagus and digestive tract. May affect behavior and urinary system, liver (hepatocellular damage, hepatic enzymes increased), blood (blood dyscrasia). May also

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are less toxic than the product itself.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Class 8: Corrosive material

Identification: : Phosphoric acid (Phosphoric Acid) UNNA: 1805 PG: III

Special Provisions for Transport: Not available.

Section 15: Other Regulatory Information

Federal and State Regulations:

Connecticut hazardous material survey.: Phosphoric Acid
Illinois toxic substances disclosure to employee act: Phosphoric acid
Illinois chemical safety act: Phosphoric acid
New York release reporting list: Phosphoric acid
Rhode Island RTK hazardous substances: Phosphoric acid
Pennsylvania RTK: Phosphoric acid
Minnesota: Phosphoric acid
Massachusetts RTK: Phosphoric acid
Massachusetts spill list: Phosphoric acid
New Jersey: Phosphoric acid
New Jersey spill list: Phosphoric acid
Louisiana spill reporting: Phosphoric acid
California Director's list of hazardous substances: Phosphoric acid
TSCA 8(b) inventory: Phosphoric Acid; Water
SARA 313 toxic chemical notification and release reporting: Phosphoric acid
CERCLA: Hazardous substances.: Phosphoric acid: 5000 lbs. (2268 kg)

Other Regulations: OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

Other Classifications:

WHMIS (Canada): CLASS E: Corrosive liquid.

DSCL (EEC):

R34- Causes burns.
S26- In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
S45- In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).

HMIS (U.S.A.):

Health Hazard: 3

Fire Hazard: 0

Reactivity: 0

Personal Protection:

National Fire Protection Association (U.S.A.):

Health: 3

Flammability: 0

Reactivity: 0

Specific hazard:

Protective Equipment:

Gloves.

Full suit.

Vapor respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate.

Face shield.

Section 16: Other Information

References: Not available.


Other Special Considerations: Not available.

Created: 10/10/2005 08:47 PM

Last Updated: 11/06/2008 12:00 PM

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MSDS Number: **P5029** * * * * *Effective Date: 08/10/04* * * * * *Supersedes: 11/02/01*

MSDS Material Safety Data Sheet	24 Hour Emergency Telephone: 908-859-2151 CHEMTREC: 1-800-424-9300
	National Response in Canada CANUTEC: 613-996-6666
From: Mallinckrodt Baker, Inc. 222 Red School Lane Phillipsburg, NJ 08865	Outside U.S. and Canada Chemtec: 703-527-3887
 Mallinckrodt CHEMICALS	J.T. Baker
NOTE: CHEMTREC, CANUTEC and National Response Center emergency numbers to be used only in the event of chemical emergencies involving a spill, leak, fire, exposure or accident involving chemicals.	
All non-emergency questions should be directed to Customer Service (1-800-582-2537) for assistance.	

POLYETHYLENE GLYCOL

1. Product Identification

Synonyms: PEG; Carbowax®; Polyglycol; Polyethylene glycol 200, 300, 400, 600,1000,1450, 3350, 4000, 6000, 8000 and 20000.

CAS No.: 25322-68-3

Molecular Weight: Not applicable to mixtures.

Chemical Formula: (C₂H₄O) n.H₂O

Product Codes:

J.T. Baker: U204, U214, U215, U216, U218, U220, U221, U222

Mallinckrodt: 7755, H273

2. Composition/Information on Ingredients

Ingredient	CAS No	Percent	Hazardous
Polyethylene Glycol	25322-68-3	90 - 100%	No

3. Hazards Identification

Emergency Overview

As part of good industrial and personal hygiene and safety procedure, avoid all unnecessary exposure to the chemical substance and ensure prompt removal from skin, eyes and clothing.

J.T. Baker SAF-T-DATA^(tm) Ratings (Provided here for your convenience)

Health Rating: 0 - None

Flammability Rating: 1 - Slight

Reactivity Rating: 0 - None

Contact Rating: 1 - Slight

Lab Protective Equip: GOGGLES; LAB COAT

Storage Color Code: Orange (General Storage)

Potential Health Effects

Inhalation:

No adverse health effects expected from inhalation. (May be a mechanical irritant.)

Ingestion:

Large doses of the lower molecular weight products may cause gastro-intestinal upset.

Skin Contact:

No adverse effects expected.

Eye Contact:

No adverse effects expected.

Chronic Exposure:

No information found.

Aggravation of Pre-existing Conditions:

Damaged skin.

4. First Aid Measures

Inhalation:

Not expected to require first aid measures.

Ingestion:

If large amounts were swallowed, give water to drink and get medical advice.

Skin Contact:

In case of contact, immediately flush skin with plenty of soap and water for at least 15 minutes. Remove contaminated clothing and shoes. Wash clothing before reuse. Get medical attention if irritation develops or persists.

Eye Contact:

In case of contact, flush eyes with plenty of water for at least 15 minutes. Get medical advice if irritation develops.

5. Fire Fighting Measures

Fire:

As with most organic solids, fire is possible at elevated temperatures or by contact with an ignition source. (increases as molecular weight increases). Flash point: 182 - 287 C.

Explosion:

Fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.

Fire Extinguishing Media:

Water spray, dry chemical, alcohol foam, or carbon dioxide.

Special Information:

In the event of a fire, wear full protective clothing and NIOSH-approved self-contained breathing apparatus with full facepiece operated in the pressure demand or other positive pressure mode.

6. Accidental Release Measures

Remove all sources of ignition. Ventilate area of leak or spill. Wear appropriate personal protective equipment as specified in Section 8.

Solid Spills: Clean up spills in a manner that does not disperse dust into the air. Use non-sparking tools and equipment. Reduce airborne dust and prevent scattering by moistening with water. Pick up spill for recovery or disposal and place in a closed container.

Liquid Spills: Absorb with vermiculite, dry sand, earth or similar material and place in a chemical waste container. Do not use combustible materials, such as saw dust. Do not flush to sewer.

7. Handling and Storage

Keep in a tightly closed container, stored in a cool, dry, ventilated area. Protect against physical damage. Containers of this material may be hazardous when empty since they retain product residues (dust, solids, vapors, liquid); observe all warnings and precautions listed for the product.

8. Exposure Controls/Personal Protection

Airborne Exposure Limits:

AIHA Workplace Environmental Exposure Level (WEEL):

Polypropylene glycols: 8-hour TWA: 10 mg/m³, as an aerosol

Ventilation System:

A system of local and/or general exhaust is recommended to keep employee exposures below the Airborne Exposure Limits. Local exhaust ventilation is generally preferred because it can control the emissions of the contaminant at its source, preventing dispersion of it into the general work area. Please refer to the ACGIH document, *Industrial Ventilation, A Manual of Recommended Practices*, most recent edition, for details.

Personal Respirators (NIOSH Approved):

For use with solids (not required for liquids): If the exposure limit is exceeded and engineering controls are not feasible, a half facepiece particulate respirator (NIOSH type N95 or better filters) may be worn for up to ten times the exposure limit or the maximum use concentration specified by the appropriate regulatory agency or respirator supplier, whichever is lowest. A full-face piece particulate respirator (NIOSH type N100 filters) may be worn up to 50 times the exposure limit, or the maximum use concentration specified by the appropriate regulatory agency, or respirator supplier, whichever is lowest. If oil particles (e.g. lubricants, cutting fluids, glycerine, etc.) are present, use a NIOSH type R or P filter. For emergencies or instances where the exposure levels are not known, use a full-facepiece positive-pressure, air-supplied respirator. **WARNING:** Air-purifying respirators do not protect workers in oxygen-deficient atmospheres.

Skin Protection:

Wear protective gloves and clean body-covering clothing.

Eye Protection:

Use chemical safety goggles. Maintain eye wash fountain and quick-drench facilities in work area.

9. Physical and Chemical Properties

Appearance:

Clear liquid or white solid.

Odor:

Mild odor.

Solubility:

Soluble in water.

Density:

range: 1.1 to 1.2 (increases as molecular weight increases)

pH:

No information found.

% Volatiles by volume @ 21C (70F):

No information found.

Boiling Point:

No information found.

Melting Point:

Melting point increases as molecular weight increases: PEG 400 = 4-8C (39-46F) PEG 600 = 20-25C (68-77F) PEG1500 = 44-48C (111-118F) PEG 4000 = 54-58C (129-136F) PEG 6000 = 56-63C (133-145F)

Vapor Density (Air=1):

No information found.

Vapor Pressure (mm Hg):

Vapor pressure is very low; as molecular weight increases, vapor pressure decreases.

Evaporation Rate (BuAc=1):

No information found.

10. Stability and Reactivity

Stability:

Stable under ordinary conditions of use and storage.

Hazardous Decomposition Products:

Carbon dioxide and carbon monoxide may form when heated to decomposition.

Hazardous Polymerization:

Will not occur.

Incompatibilities:

Incompatible with polymerization catalysts (peroxides, persulfates) and accelerators, strong oxidizers, strong bases and strong acids.

Conditions to Avoid:

Incompatibles.

11. Toxicological Information

Oral Rat LD50 for:

PEG 200 = 28gm/kg; PEG 300 = 27.5gm/kg; PEG 400 = 30.2gm/kg; PEG 600 = 30gm/kg; PEG 1000 = 32gm/kg; PEG 1450 = > 4gm/kg; PEG 4000 = 50gm/kg;

PEG 6000 = > 50gm/kg; PEG 20000 = 31.6gm/kg

Polyethylene glycol has been investigated as a mutagen; PEG 1000 has been investigated as a tumorigen.

-----\Cancer Lists\-----			
Ingredient	---NTP Carcinogen---		IARC Category
	Known	Anticipated	
Polyethylene Glycol (25322-68-3)	No	No	None

12. Ecological Information

Environmental Fate:

No information found.

Environmental Toxicity:

No information found.

13. Disposal Considerations

Whatever cannot be saved for recovery or recycling should be managed in an appropriate and approved waste disposal facility. Processing, use or contamination of this product may change the waste management options. State and local disposal regulations may differ from federal disposal regulations. Dispose of container and unused contents in accordance with federal, state and local requirements.

14. Transport Information

Not regulated.

15. Regulatory Information

-----\Chemical Inventory Status - Part 1\-----				
Ingredient	TSCA	EC	Japan	Australia
Polyethylene Glycol (25322-68-3)	Yes	No	Yes	Yes

-----\Chemical Inventory Status - Part 2\-----				
Ingredient	Korea	DSL	NDSL	Phil.
Polyethylene Glycol (25322-68-3)	Yes	Yes	No	Yes

-----\Federal, State & International Regulations - Part 1\-----				
Ingredient	-SARA 302- RQ	TPQ	-SARA 313- List	Chemical Catg.
Polyethylene Glycol (25322-68-3)	No	No	No	No

-----\Federal, State & International Regulations - Part 2\-----				
Ingredient	CERCLA	-RCRA- 261.33	-TSCA- 8(d)	
Polyethylene Glycol (25322-68-3)	No	No	No	

Chemical Weapons Convention: No TSCA 12(b): No CDTA: No
 SARA 311/312: Acute: No Chronic: No Fire: No Pressure: No
 Reactivity: No (Pure / Solid)

Australian Hazchem Code: None allocated.

Poison Schedule: None allocated.

WHMIS:

This MSDS has been prepared according to the hazard criteria of the Controlled Products Regulations (CPR) and the MSDS contains all of the information required by the CPR.

16. Other Information

NFPA Ratings: Health: 0 Flammability: 1 Reactivity: 0

Label Hazard Warning:

As part of good industrial and personal hygiene and safety procedure, avoid all unnecessary exposure to the chemical substance and ensure prompt removal from skin, eyes and clothing.

Label Precautions:

None.

Label First Aid:

Not applicable.

Product Use:

Laboratory Reagent.

Revision Information:

No Changes.

Disclaimer:

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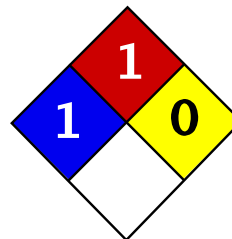
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Individuals receiving the information must exercise their independent judgment in determining its appropriateness for a particular purpose.

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Prepared by: Environmental Health & Safety

Phone Number: (314) 654-1600 (U.S.A.)



Health	1
Fire	1
Reactivity	0
Personal Protection	A

Material Safety Data Sheet POLYSORBATE 80 MSDS

Section 1: Chemical Product and Company Identification

Product Name: POLYSORBATE 80

Catalog Codes: SLP4093

CAS#: 9005-65-6

RTECS: WG2935000

TSCA: TSCA 8(b) inventory: POLYSORBATE 80

CI#: Not available.

Synonym: TWEEN 80; Polyoxyethylene 20 sorbitan monooleate; Polyethylene oxide sorbitan mono-oleate; Polyoxyethylene sorbitan monooleate; Polyoxyethylene sorbitan oleate; Sorbitan mono-9-octadecenoate poly(oxy-1,2-ethanediyl) derivatives; Sorethytan (20) monooleate

Chemical Name: Sorbitan, monooleate polyoxyethylene deriv.

Chemical Formula: Not available.

Contact Information:

Sciencelab.com, Inc.
14025 Smith Rd.
Houston, Texas 77396

US Sales: **1-800-901-7247**
International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
POLYSORBATE 80	9005-65-6	100

Toxicological Data on Ingredients: Not applicable.

Section 3: Hazards Identification

Potential Acute Health Effects: Slightly hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation.

Potential Chronic Health Effects:

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Not available.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

Repeated or prolonged exposure is not known to aggravate medical condition.

Section 4: First Aid Measures

Eye Contact:

Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention if irritation occurs.

Skin Contact:

Wash with soap and water. Cover the irritated skin with an emollient. Get medical attention if irritation develops. Cold water may be used.

Serious Skin Contact: Not available.

Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

Serious Inhalation: Not available.

Ingestion:

Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. Loosen tight clothing such as a collar, tie, belt or waistband. Get medical attention if symptoms appear.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: May be combustible at high temperature.

Auto-Ignition Temperature: Not available.

Flash Points: CLOSED CUP: >148.89°C (300°F).

Flammable Limits: Not available.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances: Slightly flammable to flammable in presence of heat.

Explosion Hazards in Presence of Various Substances:

Risks of explosion of the product in presence of mechanical impact: Not available.

Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions:

SMALL FIRE: Use DRY chemical powder.

LARGE FIRE: Use water spray, fog or foam. Do not use water jet.

Special Remarks on Fire Hazards: Not available.

Special Remarks on Explosion Hazards: Not available.

Section 6: Accidental Release Measures

Small Spill:

Dilute with water and mop up, or absorb with an inert dry material and place in an appropriate waste disposal container. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:

Absorb with an inert material and put the spilled material in an appropriate waste disposal. Finish cleaning by

spreading water on the contaminated surface and allow to evacuate through the sanitary system.

Section 7: Handling and Storage

Precautions:

Keep away from heat. Keep away from sources of ignition. Empty containers pose a fire risk, evaporate the residue under a fume hood. Ground all equipment containing material. Do not ingest. Do not breathe gas/fumes/vapor/spray. If ingested, seek medical advice immediately and show the container or the label. Keep away from incompatibles such as oxidizing agents.

Storage:

Keep container tightly closed. Keep container in a cool, well-ventilated area. Do not store above 32.2°C (90°F). Preferably store at temperatures between 50 deg F to 90 deg. F.

Section 8: Exposure Controls/Personal Protection

Engineering Controls:

Provide exhaust ventilation or other engineering controls to keep the airborne concentrations of vapors below their respective threshold limit value. Ensure that eyewash stations and safety showers are proximal to the work-station location.

Personal Protection: Safety glasses. Lab coat.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Boots. Gloves. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Liquid. (Oily liquid.)

Odor: fatty (Slight.)

Taste: Not available.

Molecular Weight: Not available.

Color: Clear Amber. Yellow.

pH (1% soln/water): 7 [Neutral.]

Boiling Point: >100°C (212°F)

Melting Point: -20.556°C (-5°F)

Critical Temperature: Not available.

Specific Gravity: 1.06 - 1.10 (Water = 1)

Vapor Pressure: <0.1 kPa (@ 20°C)

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water, methanol.

Solubility:

Easily soluble in cold water, hot water.

Soluble in methanol.

Soluble in Toluene, alcohol, cottonseed oil, corn oil, Ethyl Acetate.

Insoluble in mineral oil.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Excess heat, incompatible materials

Incompatibility with various substances: Reactive with oxidizing agents.

Corrosivity: Non-corrosive in presence of glass, of stainless steel(304), of stainless steel(316).

Special Remarks on Reactivity: Not available.

Special Remarks on Corrosivity: Not available.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Inhalation. Ingestion.

Toxicity to Animals: Acute oral toxicity (LD50): 25000 mg/kg [Mouse].

Chronic Effects on Humans: Not available.

Other Toxic Effects on Humans: Slightly hazardous in case of skin contact (irritant), of ingestion, of inhalation.

Special Remarks on Toxicity to Animals:

Lethal Dose/Conc 50% Kill:

LD50 [Rat] - Route: Oral; Dose: 34500 ul/kg

Special Remarks on Chronic Effects on Humans:

May cause adverse reproductive effects based on animal test data. No human data found.

May cause cancer based on animal test data. No human data found.

May affect genetic material (mutagenic)

Special Remarks on other Toxic Effects on Humans:

Acute Potential Health Effects:

Skin: No irritation is expected, but it may cause mild/slight irritation in more sensitive individuals. It will probably not be absorbed through the skin.

Eyes: It may cause eye irritation.

Inhalation: No expected to be a health hazard. No irritation is expected to be associated with the inhalation of this material. No toxic effects are known to be associated with the inhalation of this material.

Ingestion: This material is not likely to cause irritation upon ingestion. It is classified as "relatively harmless" by ingestion and considered to be a low ingestion hazard. Ingestion of very large doses may cause abdominal spasms and diarrhea. Animal studies have shown it to cause cardiac changes, changes in behavior (altered sleep

time) and weight loss (upon repeated or prolonged ingestion). However, no similar human data has been reported.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: Not available.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: Not applicable.

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations: TSCA 8(b) inventory: POLYSORBATE 80

Other Regulations: EINECS: This product is on the European Inventory of Existing Commercial Chemical Substances.

Other Classifications:

WHMIS (Canada): Not controlled under WHMIS (Canada).

DSCL (EEC):

This product is not classified according to the EU regulations.
Not applicable.

HMIS (U.S.A.):

Health Hazard: 1

Fire Hazard: 1

Reactivity: 0

Personal Protection: a

National Fire Protection Association (U.S.A.):

Health: 1

Flammability: 1

Reactivity: 0

Specific hazard:

Protective Equipment:

Not applicable.

Lab coat.

Not applicable.

Safety glasses.

Section 16: Other Information

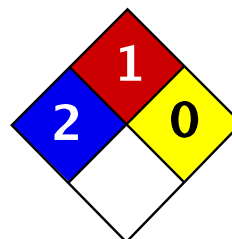
References: Not available.

Other Special Considerations: Not available.

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Health	2
Fire	1
Reactivity	0
Personal Protection	E

Material Safety Data Sheet

Sodium acetate anhydrous MSDS

Section 1: Chemical Product and Company Identification

Product Name: Sodium acetate anhydrous

Catalog Codes: SLS2710, SLS1918, SLS1123

CAS#: 127-09-3

RTECS: AJ4300010

TSCA: TSCA 8(b) inventory: Sodium acetate anhydrous

CI#: Not applicable.

Synonym: Acetic acid, sodium salt

Chemical Name: Sodium acetate

Chemical Formula: CH₃COONa

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.

Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Sodium acetate anhydrous	127-09-3	100

Toxicological Data on Ingredients: Not applicable.

Section 3: Hazards Identification

Potential Acute Health Effects:

Hazardous in case of ingestion, of inhalation. Slightly hazardous in case of skin contact (irritant), of eye contact (irritant).

Potential Chronic Health Effects:

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Not available.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

Repeated or prolonged exposure is not known to aggravate medical condition.

Section 4: First Aid Measures

Eye Contact:

Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention if irritation occurs.

Skin Contact:

Wash with soap and water. Cover the irritated skin with an emollient. Get medical attention if irritation develops. Cold water may be used.

Serious Skin Contact: Not available.

Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention if symptoms appear.

Serious Inhalation: Not available.

Ingestion:

Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. Loosen tight clothing such as a collar, tie, belt or waistband. Get medical attention if symptoms appear.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: May be combustible at high temperature.

Auto-Ignition Temperature: Not available.

Flash Points: Not available.

Flammable Limits: Not available.

Products of Combustion: These products are carbon oxides (CO, CO₂).

Fire Hazards in Presence of Various Substances:

Slightly flammable to flammable in presence of open flames and sparks, of heat.
Non-flammable in presence of shocks.

Explosion Hazards in Presence of Various Substances:

Risks of explosion of the product in presence of mechanical impact: Not available.
Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions:

SMALL FIRE: Use DRY chemical powder.
LARGE FIRE: Use water spray, fog or foam. Do not use water jet.

Special Remarks on Fire Hazards: Combustible when exposed to heat or flame.

Special Remarks on Explosion Hazards: Not available.

Section 6: Accidental Release Measures

Small Spill:

Use appropriate tools to put the spilled solid in a convenient waste disposal container. If necessary: Neutralize the residue with a dilute solution of acetic acid. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:

Use a shovel to put the material into a convenient waste disposal container. Neutralize the residue with a dilute solution of acetic acid. Finish cleaning by spreading water on the contaminated surface and allow to evacuate

through the sanitary system.

Section 7: Handling and Storage

Precautions:

Keep away from heat. Keep away from sources of ignition. Empty containers pose a fire risk, evaporate the residue under a fume hood. Ground all equipment containing material. Do not ingest. Do not breathe dust. Wear suitable protective clothing. In case of insufficient ventilation, wear suitable respiratory equipment. If ingested, seek medical advice immediately and show the container or the label. Keep away from incompatibles such as oxidizing agents, acids.

Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area.

Section 8: Exposure Controls/Personal Protection

Engineering Controls:

Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection: Safety glasses. Lab coat. Dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid. (Granular, crystalline powder.)

Odor: Odorless to acetic (Slight.)

Taste: Not available.

Molecular Weight: 82.03 g/mole

Color: Colorless. White.

pH (1% soln/water): 11 [Basic.]

Boiling Point: Not available.

Melting Point: 324°C (615.2°F)

Critical Temperature: Not available.

Specific Gravity: 1.528 (Water = 1)

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility: Easily soluble in cold water, hot water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Excess heat, incompatible materials, moisture.

Incompatibility with various substances: Reactive with oxidizing agents, acids.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity:

Hygroscopic; keep container tightly closed.

Incompatible (violent reaction) with fluorine diketene, potassium nitrate. Also incompatible with nitric acid.

Emits fumes of acetic acid upon heating and on contact with strong acids.

Special Remarks on Corrosivity: Not available.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Inhalation. Ingestion.

Toxicity to Animals:

WARNING: THE LC50 VALUES HEREUNDER ARE ESTIMATED ON THE BASIS OF A 4-HOUR EXPOSURE.

Acute oral toxicity (LD50): 3530 mg/kg [Rat].

Acute dermal toxicity (LD50): >10000 mg/kg [Rabbit].

Acute toxicity of the dust (LC50): >30000 mg/m
1 hours [Rat].

3

Chronic Effects on Humans: Not available.

Other Toxic Effects on Humans:

Hazardous in case of ingestion, of inhalation.

Slightly hazardous in case of skin contact (irritant).

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: Not available.

Special Remarks on other Toxic Effects on Humans:

Acute Potential Health Effects:

Skin: May cause skin irritation.

Eyes: May cause eye irritation.

Ingestion: May cause digestive tract irritation with abdominal pain, nausea, and vomiting. May affect behavior, and urinary system.

Inhalation: May cause respiratory tract irritation. Symptoms may include coughing, sore throat, labored breathing, and chest pain.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The product itself and its products of degradation are not toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: Not applicable.

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations: TSCA 8(b) inventory: Sodium acetate anhydrous

Other Regulations: EINECS: This product is on the European Inventory of Existing Commercial Chemical Substances.

Other Classifications:

WHMIS (Canada): Not controlled under WHMIS (Canada).

DSCL (EEC):

This product is not classified according to the EU regulations.
Not applicable.

HMIS (U.S.A.):

Health Hazard: 2

Fire Hazard: 1

Reactivity: 0

Personal Protection: E

National Fire Protection Association (U.S.A.):

Health: 2

Flammability: 1

Reactivity: 0

Specific hazard:

Protective Equipment:

Gloves.
Lab coat.
Dust respirator. Be sure to use an approved/certified respirator or equivalent.
Safety glasses.

Section 16: Other Information

References:

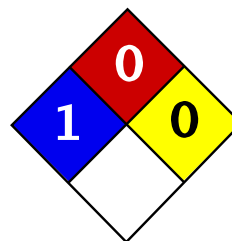
-Hawley, G.G.. The Condensed Chemical Dictionary, 11e ed., New York N.Y., Van Nostrand Reinold, 1987.
-SAX, N.I. Dangerous Properties of Industrial Materials. Toronto, Van Nostrand Reinold, 6e ed. 1984.
-The Sigma-Aldrich Library of Chemical Safety Data, Edition II.
Registry of Toxic Effects of Chemical Substances.
Hazardous Substance Data Bank.

Other Special Considerations: Not available.

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Last Updated: 10/09/2005 06:28 PM

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Health	1
Fire	0
Reactivity	0
Personal Protection	E

Material Safety Data Sheet

Sodium bicarbonate MSDS

Section 1: Chemical Product and Company Identification

Product Name: Sodium bicarbonate

Catalog Codes: SLS3241, SLS2446, SLS3868

CAS#: 144-55-8

RTECS: VZ0950000

TSCA: TSCA 8(b) inventory: Sodium bicarbonate

CI#: Not available.

Synonym: Baking Soda; Bicarbonate of soda; Sodium acid carbonate; Monosodium carbonate; Sodium hydrogen carbonate; Carbonic acid monosodium salt

Chemical Name: Sodium Bicarbonate

Chemical Formula: NaHCO₃

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.

Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Sodium bicarbonate	144-55-8	100

Toxicological Data on Ingredients: Not applicable.

Section 3: Hazards Identification

Potential Acute Health Effects: Slightly hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation.

Potential Chronic Health Effects:

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Not available.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

Repeated or prolonged exposure is not known to aggravate medical condition.

Section 4: First Aid Measures

Eye Contact:

Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention if irritation occurs.

Skin Contact:

Wash with soap and water. Cover the irritated skin with an emollient. Get medical attention if irritation develops. Cold water may be used.

Serious Skin Contact: Not available.

Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

Serious Inhalation: Not available.

Ingestion:

Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. Loosen tight clothing such as a collar, tie, belt or waistband. Get medical attention if symptoms appear.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: Non-flammable.

Auto-Ignition Temperature: Not applicable.

Flash Points: Not applicable.

Flammable Limits: Not applicable.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances: Not applicable.

Explosion Hazards in Presence of Various Substances:

Risks of explosion of the product in presence of mechanical impact: Not available.

Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions: Not applicable.

Special Remarks on Fire Hazards: When heated to decomposition it emits acrid smoke and irritating fumes.

Special Remarks on Explosion Hazards: Not available.

Section 6: Accidental Release Measures

Small Spill:

Use appropriate tools to put the spilled solid in a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:

Use a shovel to put the material into a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and allow to evacuate through the sanitary system.

Section 7: Handling and Storage

Precautions:

Do not ingest. Do not breathe dust. If ingested, seek medical advice immediately and show the container or the label. Keep away from incompatibles such as acids.

Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area.

Section 8: Exposure Controls/Personal Protection

Engineering Controls:

Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection: Safety glasses. Lab coat. Dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid.

Odor: Odorless.

Taste: Saline. Alkaline.

Molecular Weight: 84.01g/mole

Color: White.

pH (1% soln/water): Not available.

Boiling Point: Not available.

Melting Point: Not available.

Critical Temperature: Not available.

Specific Gravity: Density: 2.159 (Water = 1)

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility:

Soluble in cold water.

Slightly soluble in alcohol.

Solubility in Water: 6.4, 7.6, 8.7, 10.0, 11.3, 12.7, 14.2, 16.5, 19.1 g/100 solution at 0, 10, 20, 30, 40, 50, 60, 80, and 100 deg. C, respectively.

Solubility in Water: 6.9, 8.2, 9.6, 11.1, 12.7, 14.5, 16.5, 19.7, and 23.6 g/100g water at 0, 10, 20, 30, 40, 50, 60, 80, 100 deg. C, respectively.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Incompatible materials, Moisture. Stable in dry air, but slowly decomposes in moist air.

Incompatibility with various substances: Reactive with acids.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity:

Reacts with acids to form carbon dioxide.

Dangerous reaction with monoammonium phosphate or a sodium-potassium alloy.

Special Remarks on Corrosivity: Not available.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Inhalation. Ingestion.

Toxicity to Animals: Acute oral toxicity (LD50): 3360 mg/kg [Mouse].

Chronic Effects on Humans: Not available.

Other Toxic Effects on Humans: Slightly hazardous in case of skin contact (irritant), of ingestion, of inhalation.

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans:

Sodium Bicarbonate as produced genetic effects in rats (unscheduled DNA synthesis). However, no effects have been found in humans.

Special Remarks on other Toxic Effects on Humans:

Acute Potential Health Effects:

Skin: May cause mild skin irritation.

Eyes: May cause mild eye irritation.

Inhalation: May cause respiratory tract irritation. Symptoms may include coughing and sneezing.

Ingestion: Symptoms of overexposure to Sodium Bicarbonate include thirst, abdominal pain, gastroenteritis, and inflammation of the digestive tract.

Chronic Potential Health Effects:

Skin: Repeated or prolonged skin contact may cause irritation, drying or cracking of the skin.

Ingestion and Inhalation: Chronic toxicity usually occurs within 4 to 10 days following ingestion of very large amounts. Repeated or prolonged ingestion or inhalation of large amounts may cause metabolic abnormalities, and sodium retention. Metabolic abnormalities such as acidosis, hypernatremia, hyponatremia, alkalosis, hypocalcemia, or sodium retention may affect the blood, kidneys, respiration (cyanosis, apnea secondary to metabolic acidosis or pulmonary edema), and cardiovascular system (tachycardia, hypotension).

Severe toxicity may also affect behavior/central nervous system/nervous system. Neurological changes may

result from metabolic abnormalities. These may include fatigue, irritability, dizziness, mental confusion, paresthesia, seizures, tetany, cerebral edema

Medical Conditions Aggravated by Exposure: Persons with pre-existing skin conditions might have increased sensitivity. Predisposing conditions that contribute to a mild alkali syndrome include, renal disease, dehydration, and electrolyte imbalance, hypertension, sarcoidosis, congestive heart failure, edema, or other sodium retaining conditions.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The product itself and its products of degradation are not toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: Not applicable.

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations: TSCA 8(b) inventory: Sodium bicarbonate

Other Regulations: Not available.

Other Classifications:

WHMIS (Canada): Not controlled under WHMIS (Canada).

DSCL (EEC):

This product is not classified according to the EU regulations.
Not applicable.

HMIS (U.S.A.):

Health Hazard: 1

Fire Hazard: 0

Reactivity: 0

Personal Protection: E

National Fire Protection Association (U.S.A.):

Health: 1

Flammability: 0

Reactivity: 0

Specific hazard:

Protective Equipment:

Gloves.

Lab coat.

Dust respirator. Be sure to use an approved/certified respirator or equivalent.

Safety glasses.

Section 16: Other Information

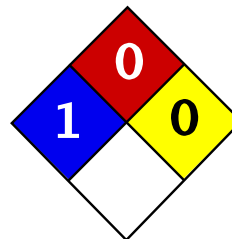
References: Not available.

Other Special Considerations: Not available.

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Last Updated: 11/06/2008 12:00 PM

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Health	1
Fire	1
Reactivity	0
Personal Protection	E

Material Safety Data Sheet

Sodium citrate dihydrate MSDS

Section 1: Chemical Product and Company Identification

Product Name: Sodium citrate dihydrate

Catalog Codes: SLS4237, SLS3442, SLS1225

CAS#: 6132-04-3

RTECS: GE8300000 (Sodium Citrate, anhydrous)

TSCA: TSCA 8(b) inventory: No products were found.

CI#: Not available.

Synonym: Citnatin, Citreme, Citrosoedine, Citrosodna, Natrocital; Trisodium citrate dihydrate; 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, trisodium salt, dihydrate

Chemical Name: Citric acid, trisodium salt, dihydrate

Chemical Formula: C₆H₅Na₃O₇·2H₂O

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.

Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Sodium citrate dihydrate	6132-04-3	100

Toxicological Data on Ingredients: Not applicable.

Section 3: Hazards Identification

Potential Acute Health Effects: Slightly hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation.

Potential Chronic Health Effects:

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Not available.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

Repeated or prolonged exposure is not known to aggravate medical condition.

Section 4: First Aid Measures

Eye Contact:

Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention if irritation occurs.

Skin Contact:

Wash with soap and water. Cover the irritated skin with an emollient. Get medical attention if irritation develops. Cold water may be used.

Serious Skin Contact: Not available.

Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

Serious Inhalation: Not available.

Ingestion:

Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. If large quantities of this material are swallowed, call a physician immediately. Loosen tight clothing such as a collar, tie, belt or waistband.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: May be combustible at high temperature.

Auto-Ignition Temperature: Not available.

Flash Points: Not available.

Flammable Limits: Not available.

Products of Combustion: These products are carbon oxides (CO, CO₂). Some metallic oxides.

Fire Hazards in Presence of Various Substances:

Slightly flammable to flammable in presence of heat.

Non-flammable in presence of shocks.

Explosion Hazards in Presence of Various Substances:

Slightly explosive in presence of open flames and sparks.

Non-explosive in presence of shocks.

Fire Fighting Media and Instructions:

SMALL FIRE: Use DRY chemical powder.

LARGE FIRE: Use water spray, fog or foam. Do not use water jet.

Special Remarks on Fire Hazards: As with most organic solids, fire is possible at elevated temperatures

Special Remarks on Explosion Hazards:

Fine dust dispersed in air in sufficient concentrations, and in the presences of an ignition source is a potential dust explosion hazard.

Section 6: Accidental Release Measures

Small Spill:

Use appropriate tools to put the spilled solid in a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:

Use a shovel to put the material into a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and allow to evacuate through the sanitary system.

Section 7: Handling and Storage**Precautions:**

Keep away from heat. Keep away from sources of ignition. Do not breathe dust. Keep away from incompatibles such as oxidizing agents.

Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area.

Section 8: Exposure Controls/Personal Protection**Engineering Controls:**

Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection: Safety glasses. Lab coat. Dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid. (Crystalline granules solid.)

Odor: Odorless.

Taste: Cool, Saline.

Molecular Weight: 294.1 g/mole

Color: White.

pH (1% soln/water):

8 [Basic.] The aqueous solution is slightly alkaline to litmus; pH about 8

Boiling Point: Not available.

Melting Point: Not available.

Critical Temperature: Not available.

Specific Gravity: Not available.

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility:

Easily soluble in hot water.

Soluble in cold water.

Insoluble in alcohol.

Soluble in 1.3 parts water.

Soluble in 0.6 parts boiling water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Excess heat, dust generation, incompatible materials

Incompatibility with various substances: Reactive with oxidizing agents.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity: Decomposes at red heat. Becomes anhydrous at 150 deg. C

Special Remarks on Corrosivity: Not available.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Inhalation. Ingestion.

Toxicity to Animals:

LD50: Not available.

LC50: Not available.

Chronic Effects on Humans: Not available.

Other Toxic Effects on Humans: Slightly hazardous in case of skin contact (irritant), of ingestion, of inhalation.

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: Not available.

Special Remarks on other Toxic Effects on Humans:

Potential Health Effects:

Skin: Possible irritation on prolonged contact with moist or sensitive areas of the skin.

Eyes: No adverse effects expected, but dust may cause mechanical irritation.

Inhalation: Inhalation of large amounts of dust may cause irritation to the respiratory tract. Low hazard for usual industrial handling.

Ingestion: Ingestion of large amounts may cause gastrointestinal tract irritation/disturbances.

May affect behavior (convulsions), respiration (cyanosis).

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The product itself and its products of degradation are not toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: Not applicable.

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations: No products were found.

Other Regulations: Not available.

Other Classifications:

WHMIS (Canada): Not controlled under WHMIS (Canada).

DSCL (EEC):

This product is not classified according to the EU regulations.
S24/25- Avoid contact with skin and eyes.

HMIS (U.S.A.):

Health Hazard: 1

Fire Hazard: 1

Reactivity: 0

Personal Protection: E

National Fire Protection Association (U.S.A.):

Health: 1

Flammability: 0

Reactivity: 0

Specific hazard:

Protective Equipment:

Gloves.
Lab coat.
Dust respirator. Be sure to use an approved/certified respirator or equivalent.
Safety glasses.

Section 16: Other Information

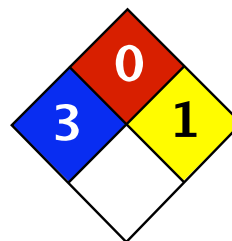
References: Not available.

Other Special Considerations: Not available.

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Last Updated: 11/06/2008 12:00 PM

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Health	3
Fire	0
Reactivity	2
Personal Protection	J

Material Safety Data Sheet

Sodium hydroxide MSDS

Section 1: Chemical Product and Company Identification

Product Name: Sodium hydroxide

Catalog Codes: SLS3298, SLS1081, SLS2503, SLS3925, SLS1705

CAS#: 1310-73-2

RTECS: WB4900000

TSCA: TSCA 8(b) inventory: Sodium hydroxide

CI#: Not available.

Synonym: Caustic Soda

Chemical Name: Sodium Hydroxide

Chemical Formula: NaOH

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.
Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Sodium hydroxide	1310-73-2	100

Toxicological Data on Ingredients: Sodium hydroxide LD50: Not available. LC50: Not available.

Section 3: Hazards Identification

Potential Acute Health Effects:

Very hazardous in case of skin contact (corrosive, irritant, permeator), of eye contact (irritant, corrosive), of ingestion, of inhalation. The amount of tissue damage depends on length of contact. Eye contact can result in corneal damage or blindness. Skin contact can produce inflammation and blistering. Inhalation of dust will produce irritation to gastro-intestinal or respiratory tract, characterized by burning, sneezing and coughing. Severe over-exposure can produce lung damage, choking, unconsciousness or death. Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering.

Potential Chronic Health Effects:

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

The substance may be toxic to mucous membranes, upper respiratory tract, skin, eyes. Repeated or prolonged exposure to the substance can produce target organs damage. Repeated exposure of the eyes to a low level of dust can produce eye irritation. Repeated skin exposure can produce local skin destruction, or dermatitis. Repeated inhalation of dust can produce varying degree of respiratory irritation or lung damage.

Section 4: First Aid Measures

Eye Contact:

Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention immediately.

Skin Contact:

In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Cover the irritated skin with an emollient. Cold water may be used. Wash clothing before reuse. Thoroughly clean shoes before reuse. Get medical attention immediately.

Serious Skin Contact:

Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek medical attention.

Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.

Serious Inhalation:

Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. If breathing is difficult, administer oxygen. If the victim is not breathing, perform mouth-to-mouth resuscitation. **WARNING:** It may be hazardous to the person providing aid to give mouth-to-mouth resuscitation when the inhaled material is toxic, infectious or corrosive. Seek immediate medical attention.

Ingestion:

Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. If large quantities of this material are swallowed, call a physician immediately. Loosen tight clothing such as a collar, tie, belt or waistband.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: Non-flammable.

Auto-Ignition Temperature: Not applicable.

Flash Points: Not applicable.

Flammable Limits: Not applicable.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances: metals

Explosion Hazards in Presence of Various Substances:

Risks of explosion of the product in presence of mechanical impact: Not available.

Risks of explosion of the product in presence of static discharge: Not available.

Slightly explosive in presence of heat.

Fire Fighting Media and Instructions: Not available

Special Remarks on Fire Hazards:

sodium hydroxide + zinc metal dust causes ignition of the latter.

Under proper conditions of temperature, pressure and state of division, it can ignite or react violently with acetaldehyde, allyl alcohol, allyl chloride, benzene-1,4-diol, chlorine trifluoride, 1,2 dichloroethylene, nitroethane, nitromethane, nitroparaffins, nitropropane, cinnamaldehyde, 2,2-dichloro-3,3-dimethylbutane. Sodium hydroxide in contact with water may generate enough heat to ignite adjacent combustible materials. Phosphorous boiled with NaOH yields mixed phosphines which may ignite spontaneously in air. sodium hydroxide and cinnamaldehyde + heat may cause ignition. Reaction with certain metals releases flammable and explosive hydrogen gas.

Special Remarks on Explosion Hazards:

Sodium hydroxide reacts to form explosive products with ammonia + silver nitrate. Benzene extract of allyl benzenesulfonate prepared from allyl alcohol, and benzene sulfonyl chloride in presence of aqueous sodium hydroxide, under vacuum distillation, residue darkened and exploded. Sodium Hydroxide + impure tetrahydrofuran, which can contain peroxides, can cause serious explosions. Dry mixtures of sodium hydroxide and sodium tetrahydroborate liberate hydrogen explosively at 230-270 deg. C. Sodium Hydroxide reacts with sodium salt of trichlorophenol + methyl alcohol + trichlorobenzene + heat to cause an explosion.

Section 6: Accidental Release Measures

Small Spill:

Use appropriate tools to put the spilled solid in a convenient waste disposal container. If necessary: Neutralize the residue with a dilute solution of acetic acid.

Large Spill:

Corrosive solid.

Stop leak if without risk. Do not get water inside container. Do not touch spilled material. Use water spray to reduce vapors. Prevent entry into sewers, basements or confined areas; dike if needed. Call for assistance on disposal. Neutralize the residue with a dilute solution of acetic acid. Be careful that the product is not present at a concentration level above TLV. Check TLV on the MSDS and with local authorities.

Section 7: Handling and Storage

Precautions:

Keep container dry. Do not breathe dust. Never add water to this product. In case of insufficient ventilation, wear suitable respiratory equipment. If you feel unwell, seek medical attention and show the label when possible. Avoid contact with skin and eyes. Keep away from incompatibles such as oxidizing agents, reducing agents, metals, acids, alkalis, moisture.

Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area. Hygroscopic. Deliquescent.

Section 8: Exposure Controls/Personal Protection

Engineering Controls:

Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection:

Splash goggles. Synthetic apron. Vapor and dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Vapor and dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits:

STEL: 2 (mg/m³) from ACGIH (TLV) [United States]

TWA: 2 CEIL: 2 (mg/m³) from OSHA (PEL) [United States]
CEIL: 2 (mg/m³) from NIOSH Consult local authorities for acceptable exposure limits.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid. (Deliquescent solid.)

Odor: Odorless.

Taste: Not available.

Molecular Weight: 40 g/mole

Color: White.

pH (1% soln/water): 13.5 [Basic.]

Boiling Point: 1388°C (2530.4°F)

Melting Point: 323°C (613.4°F)

Critical Temperature: Not available.

Specific Gravity: 2.13 (Water = 1)

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility: Easily soluble in cold water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Incompatible materials, moisture, moist air

Incompatibility with various substances:

Highly reactive with metals.

Reactive with oxidizing agents, reducing agents, acids, alkalis, moisture.

Corrosivity: Not available.

Special Remarks on Reactivity:

Hygroscopic. Much heat is evolved when solid material is dissolved in water. Therefore cold water and caution must be used for this process.

Sodium hydroxide solution and octanol + diborane during a work-up of a reaction mixture of oxime and diborane in tetrahydrofuran is very exothermic, a mild explosion being noted on one occasion.

Reactive with water, acids (mineral, non-oxidizing, e.g. hydrochloric, hydrofluoric acid, muriatic acid, phosphoric), acids (mineral, oxidizing e.g. chromic acid, hypochlorous acid, nitric acid, sulfuric acid), acids (organic e.g. acetic acid, benzoic acid, formic acid, methanoic acid, oxalic acid), aldehydes (e.g. acetaldehyde, acrolein, chloral hydrate, formaldehyde), carbamates (e.g. carbanolate, carbofuran), esters (e.g. butyl acetate, ethyl acetate, propyl formate), halogenated organics (dibromoethane, hexachlorobenzene, methyl chloride, trichloroethylene), isocyanates (e.g. methyl isocyanate), ketones (acetone, acetophenone, MEK, MIBK), acid chlorides, strong bases, strong oxidizing agents, strong reducing agents, flammable liquids, powdered metals and metals (i.e. aluminum, tin, zinc, hafnium, raney nickel), metals (alkali and alkaline e.g. cesium, potassium, sodium), metal compounds (toxic e.g. beryllium, lead acetate, nickel carbonyl, tetraethyl lead), nitrides (e.g. potassium nitride, sodium nitride), nitriles (e.g. acetonitrile, methyl cyanide), nitro compounds (organic e.g. nitrobenzene, nitromethane), acetic anhydride, chlorohydrin, chlorosulfonic acid, ethylene cyanohydrin, glyoxal, hydrosulfuric acid, oleum, propiolactone, acrylonitrile, phosphorus pentoxide, chloroethanol, chloroform-methanol, tetrahydroborate, cyanogen azide, 1,2,4,5 tetrachlorobenzene, cinnamaldehyde.
Reacts with formaldehyde hydroxide to yield formic acid, and hydrogen.

Special Remarks on Corrosivity: Very caustic to aluminum and other metals in presence of moisture.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Absorbed through skin. Dermal contact. Eye contact. Inhalation. Ingestion.

Toxicity to Animals:

LD50: Not available.

LC50: Not available.

Chronic Effects on Humans:

MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells.

May cause damage to the following organs: mucous membranes, upper respiratory tract, skin, eyes.

Other Toxic Effects on Humans:

Extremely hazardous in case of inhalation (lung corrosive).

Very hazardous in case of skin contact (corrosive, irritant, permeator), of eye contact (corrosive), of ingestion, .

Special Remarks on Toxicity to Animals:

Lowest Published Lethal Dose:

LDL [Rabbit] - Route: Oral; Dose: 500 mg/kg

Special Remarks on Chronic Effects on Humans: May affect genetic material. Investigation as a mutagen (cytogenetic analysis)

Special Remarks on other Toxic Effects on Humans:

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The product itself and its products of degradation are not toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Class 8: Corrosive material

Identification: : Sodium hydroxide, solid UNNA: 1823 PG: II

Special Provisions for Transport: Not available.

Section 15: Other Regulatory Information

Federal and State Regulations:

Illinois toxic substances disclosure to employee act: Sodium hydroxide

Illinois chemical safety act: Sodium hydroxide

New York release reporting list: Sodium hydroxide

Rhode Island RTK hazardous substances: Sodium hydroxide

Pennsylvania RTK: Sodium hydroxide

Minnesota: Sodium hydroxide

Massachusetts RTK: Sodium hydroxide

New Jersey: Sodium hydroxide

Louisiana spill reporting: Sodium hydroxide

California Director's List of Hazardous Substances: Sodium hydroxide

TSCA 8(b) inventory: Sodium hydroxide

CERCLA: Hazardous substances.: Sodium hydroxide: 1000 lbs. (453.6 kg)

Other Regulations:

OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

EINECS: This product is on the European Inventory of Existing Commercial Chemical Substances.

Other Classifications:

WHMIS (Canada): CLASS E: Corrosive solid.

DSCL (EEC):

R35- Causes severe burns.

S26- In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

S37/39- Wear suitable gloves and eye/face protection.

S45- In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).

HMIS (U.S.A.):

Health Hazard: 3

Fire Hazard: 0

Reactivity: 2

Personal Protection: j

National Fire Protection Association (U.S.A.):

Health: 3

Flammability: 0

Reactivity: 1

Specific hazard:

Protective Equipment:

Gloves.

Synthetic apron.

Vapor and dust respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate.

Splash goggles.

Section 16: Other Information

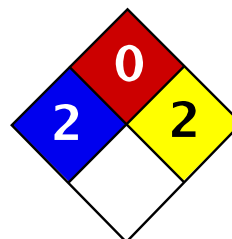
References: Not available.

Other Special Considerations: Not available.

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Health	2
Fire	0
Reactivity	0
Personal Protection	C

Material Safety Data Sheet

Sodium phosphate tribasic MSDS

Section 1: Chemical Product and Company Identification

Product Name: Sodium phosphate tribasic

Catalog Codes: SLS2650, SLS4072

CAS#: 7601-54-9

RTECS: TC9490000

TSCA: TSCA 8(b) inventory: Sodium phosphate tribasic

CI#: Not available.

Synonym: Trisodium Phosphate Anhydrous; Phosphoric Acid, Trisodium Salt; Trisodium Orthophosphate

Chemical Name: Sodium Phosphate Tribasic

Chemical Formula: Na₃PO₄

Contact Information:

Sciencelab.com, Inc.

14025 Smith Rd.

Houston, Texas 77396

US Sales: **1-800-901-7247**

International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Sodium phosphate tribasic	7601-54-9	100

Toxicological Data on Ingredients: Sodium phosphate tribasic: ORAL (LD50): Acute: 4150 mg/kg [Rat [information from other supplier]]. DERMAL (LD50): Acute: >7940 mg/kg [Rabbit [information from other supplier]]. >300 mg/kg [Rabbit [Registry of Toxic Effects of Chemical Substances database]].

Section 3: Hazards Identification

Potential Acute Health Effects:

Hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation. Slightly hazardous in case of skin contact (permeator). Corrosive to eyes and skin. The amount of tissue damage depends on length of contact. Eye contact can result in corneal damage or blindness. Skin contact can produce inflammation and blistering. Inhalation of dust will produce irritation to gastro-intestinal or respiratory tract, characterized by burning, sneezing and coughing. Severe over-exposure can produce lung damage, choking, unconsciousness or death.

Potential Chronic Health Effects:

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Not available.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

Repeated exposure of the eyes to a low level of dust can produce eye irritation. Repeated skin exposure can produce local skin destruction, or dermatitis. Repeated inhalation of dust can produce varying degree of respiratory irritation or lung damage.

Section 4: First Aid Measures

Eye Contact:

Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention immediately.

Skin Contact:

In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Cover the irritated skin with an emollient. Cold water may be used. Wash clothing before reuse. Thoroughly clean shoes before reuse. Get medical attention immediately.

Serious Skin Contact:

Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek medical attention.

Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.

Serious Inhalation: Not available.

Ingestion:

Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. Loosen tight clothing such as a collar, tie, belt or waistband. Get medical attention if symptoms appear.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: Non-flammable.

Auto-Ignition Temperature: Not applicable.

Flash Points: Not applicable.

Flammable Limits: Not applicable.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances: Not applicable.

Explosion Hazards in Presence of Various Substances:

Risks of explosion of the product in presence of mechanical impact: Not available.

Risks of explosion of the product in presence of static discharge: Not available.

Slightly explosive in presence of heat.

Fire Fighting Media and Instructions: Not applicable.

Special Remarks on Fire Hazards: Not available.

Special Remarks on Explosion Hazards: Containers may explode when heated

Section 6: Accidental Release Measures

Small Spill:

Use appropriate tools to put the spilled solid in a convenient waste disposal container. If necessary: Neutralize the residue with a dilute solution of acetic acid. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:

Corrosive solid.

Stop leak if without risk. Do not get water inside container. Do not touch spilled material. Use water spray to reduce vapors. Prevent entry into sewers, basements or confined areas; dike if needed. Call for assistance on disposal. Neutralize the residue with a dilute solution of acetic acid. Be careful that the product is not present at a concentration level above TLV. Check TLV on the MSDS and with local authorities.

Section 7: Handling and Storage

Precautions:

Keep container dry. Do not ingest. Do not breathe dust. Never add water to this product. Wear suitable protective clothing. In case of insufficient ventilation, wear suitable respiratory equipment. If ingested, seek medical advice immediately and show the container or the label. Avoid contact with skin and eyes. Keep away from incompatibles such as moisture.

Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area. Do not store above 23°C (73.4°F).

Section 8: Exposure Controls/Personal Protection

Engineering Controls:

Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection: Safety glasses. Synthetic apron. Gloves (impervious).

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Boots. Gloves. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits:

TWA: 15 (mg/m³) from OSHA (PEL) [United States] Inhalation Total.

TWA: 5 (mg/m³) from OSHA (PEL) [United States] Inhalation Respirable.

TWA: 5 STEL: 5 (mg/m³) from AIHA Inhalation Consult local authorities for acceptable exposure limits.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid.

Odor: Odorless.

Taste: Not available.

Molecular Weight: 163.94 g/mole

Color: White.

pH (1% soln/water): 11.9 [Basic.]

Boiling Point: Not available.

Melting Point: 75°C (167°F)

Critical Temperature: Not available.

Specific Gravity: 1.62 (Water = 1)

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility:

Easily soluble in hot water.

Soluble in cold water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Moisture

Incompatibility with various substances: Reactive with moisture.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity: Hygroscopic. Sodium Phosphate Tribasic forms a strong caustic solution similar to soda lye

Special Remarks on Corrosivity: When wet, mild steel and brass may be corroded by sodium phosphate tribasic.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Absorbed through skin. Inhalation. Ingestion.

Toxicity to Animals:

Acute oral toxicity (LD50): 4150 mg/kg [Rat [information from other supplier]].

Acute dermal toxicity (LD50): >300 mg/kg [Rabbit [Registry of Toxic Effects of Chemical Substances database]].

Chronic Effects on Humans: Not available.

Other Toxic Effects on Humans:

Extremely hazardous in case of skin contact (corrosive), of eye contact (corrosive), of inhalation (lung corrosive).

Hazardous in case of skin contact (irritant), of ingestion, .

Slightly hazardous in case of skin contact (permeator).

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: May affect genetic material (mutagenic)

Special Remarks on other Toxic Effects on Humans:

Acute Potential Health Effects:

Skin: Causes skin irritation with possible burning pain and corrosive damage. It may be absorbed through the skin.

Eyes: Causes eye irritation. It causes immediate and severe pain followed by conjunctival edema and corneal clouding. Later cataract formation may occur. This substance may cause eye burns.

Inhalation: May be harmful if inhaled. Inhalation of dust may Cause respiratory tract and mucous membrane irritation with coughing, sneezing, choking, difficulty breathing, and pulmonary edema.

Ingestion: May be harmful if swallowed. May cause severe gastrointestinal (digestive) tract irritation with severe nausea, vomiting, abdominal discomfort, violent purging, diarrhea, and burning sensation. Ingestion of large amounts may induce hypocalcemia or hyponatremia characterized by tetanus-like spasms, due to the sequestration of calcium ions by the phosphate moiety. It may also cause caustic burns of the mouth oropharynx, esophagus, or gastrointestinal tract.

Section 12: Ecological Information

Ecotoxicity:

Ecotoxicity in water (LC50): 220 mg/l 96 hours [Bluegill sunfish]. 120 mg/l 96 hours [Rainbow Trout]. 177 mg/l 50 hours [Daphnia].

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are as toxic as the original product.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: : Not available. UNNA: 9148 PG: III

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations:

New York release reporting list: Sodium phosphate tribasic

Pennsylvania RTK: Sodium phosphate tribasic

Minnesota: Sodium phosphate tribasic

Massachusetts RTK: Sodium phosphate tribasic

New Jersey: Sodium phosphate tribasic

California Director's List of Hazardous Substances: Sodium phosphate tribasic

TSCA 8(b) inventory: Sodium phosphate tribasic

CERCLA: Hazardous substances.: Sodium phosphate tribasic: 5000 lbs. (2268 kg)

Other Regulations:

OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

EINECS: This product is on the European Inventory of Existing Commercial Chemical Substances.

Other Classifications:

WHMIS (Canada): CLASS E: Corrosive solid.

DSCL (EEC):

R35- Causes severe burns.

S1/2- Keep locked up and out of the reach of children.

S26- In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

S36/37- Wear suitable protective clothing and gloves.

S39- Wear eye/face protection.

S45- In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).

HMIS (U.S.A.):

Health Hazard: 2

Fire Hazard: 0

Reactivity: 0

Personal Protection: C

National Fire Protection Association (U.S.A.):

Health: 2

Flammability: 0

Reactivity: 2

Specific hazard:

Protective Equipment:

Gloves (impervious).

Synthetic apron.

Wear appropriate respirator when ventilation is inadequate.

Safety glasses.

Section 16: Other Information

References: Not available.

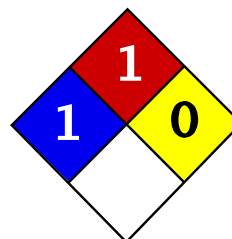
Other Special Considerations: Not available.

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Last Updated: 11/06/2008 12:00 PM

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Health	1
Fire	1
Reactivity	0
Personal Protection	E

Material Safety Data Sheet

Tris(hydroxymethyl)amino methane HCl MSDS

Section 1: Chemical Product and Company Identification

Product Name: Tris(hydroxymethyl)amino methane HCl

Catalog Codes: SLT1672

CAS#: 1185-53-1

RTECS: Not available.

TSCA: TSCA 8(b) inventory: Tris(hydroxymethyl)amino methane HCl

CI#: Not available.

Synonym: Spectris Hydrochloride Tris(hydroxymethyl)amino methane HCl
2-Amino-2-(hydroxymethyl)propane-1,3-diol hydrochloride

Chemical Name: 1,3-Propanediol,
2-amino-2-(hydroxymethyl)-, hydrochloride

Chemical Formula: C₄H₁₁N-O₃.HCl

Contact Information:

Sciencelab.com, Inc.
14025 Smith Rd.
Houston, Texas 77396

US Sales: **1-800-901-7247**
International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Tris(hydroxymethyl)amino methane HCl	1185-53-1	100

Toxicological Data on Ingredients: Not applicable.

Section 3: Hazards Identification

Potential Acute Health Effects: Slightly hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation.

Potential Chronic Health Effects:

CARCINOGENIC EFFECTS: Not available.

MUTAGENIC EFFECTS: Not available.

TERATOGENIC EFFECTS: Not available.

DEVELOPMENTAL TOXICITY: Not available.

Repeated or prolonged exposure is not known to aggravate medical condition.

Section 4: First Aid Measures

Eye Contact:

Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention if irritation occurs.

Skin Contact:

Wash with soap and water. Cover the irritated skin with an emollient. Get medical attention if irritation develops. Cold water may be used.

Serious Skin Contact: Not available.

Inhalation:

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

Serious Inhalation: Not available.

Ingestion:

Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. If large quantities of this material are swallowed, call a physician immediately. Loosen tight clothing such as a collar, tie, belt or waistband.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: May be combustible at high temperature.

Auto-Ignition Temperature: Not available.

Flash Points: Not available.

Flammable Limits: Not available.

Products of Combustion: These products are carbon oxides (CO, CO₂), nitrogen oxides (NO, NO₂...).

Fire Hazards in Presence of Various Substances:

Slightly flammable to flammable in presence of heat.

Non-flammable in presence of shocks.

Explosion Hazards in Presence of Various Substances:

Risks of explosion of the product in presence of mechanical impact: Not available.

Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions:

SMALL FIRE: Use DRY chemical powder.

LARGE FIRE: Use water spray, fog or foam. Do not use water jet.

Special Remarks on Fire Hazards: As with most organic solids, fire is possible at elevated temperatures

Special Remarks on Explosion Hazards: Not available.

Section 6: Accidental Release Measures

Small Spill:

Use appropriate tools to put the spilled solid in a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:

Use a shovel to put the material into a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and allow to evacuate through the sanitary system.

Section 7: Handling and Storage

Precautions:

Keep away from heat. Keep away from sources of ignition. Ground all equipment containing material. Do not breathe dust. Keep away from incompatibles such as oxidizing agents.

Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area.

Section 8: Exposure Controls/Personal Protection

Engineering Controls:

Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection: Safety glasses. Lab coat. Dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:

Splash goggles. Full suit. Dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid. (Crystals solid.)

Odor: Not available.

Taste: Not available.

Molecular Weight: 157.59 g/mole

Color: White.

pH (1% soln/water): Not available.

Boiling Point: Not available.

Melting Point: 150°C (302°F)

Critical Temperature: Not available.

Specific Gravity: Not available.

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility: Soluble in cold water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Excess heat, incompatible materials, moisture

Incompatibility with various substances: Reactive with oxidizing agents.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity: Hygroscopic; keep container tightly closed.

Special Remarks on Corrosivity: Not available.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Inhalation. Ingestion.

Toxicity to Animals:

LD50: Not available.

LC50: Not available.

Chronic Effects on Humans: Not available.

Other Toxic Effects on Humans: Slightly hazardous in case of skin contact (irritant), of ingestion, of inhalation.

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: Not available.

Special Remarks on other Toxic Effects on Humans:

Acute Potential Health Effects:

Skin: May cause skin irritation with redness, and skin inflammation.

Eyes: May cause eye irritation.

Inhalation: Excessive inhalation may cause respiratory tract and mucous membrane irritation, coughing, and shortness of breath. No toxicity expected from inhalation.

Ingestion: Ingestion of excessive amounts may cause nausea, vomiting, diarrhea. It may also cause weakness, collapse and coma.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:

Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The product itself and its products of degradation are not toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: Not applicable.

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations: TSCA 8(b) inventory: Tris(hydroxymethyl)amino methane HCl

Other Regulations: EINECS: This product is on the European Inventory of Existing Commercial Chemical Substances.

Other Classifications:

WHMIS (Canada): Not controlled under WHMIS (Canada).

DSCL (EEC):

R36/37/38- Irritating to eyes,
respiratory system and skin.

S22- Do not breathe dust.

S24/25- Avoid contact with skin and eyes.

S36/37- Wear suitable protective clothing and
gloves.

HMIS (U.S.A.):

Health Hazard: 1

Fire Hazard: 1

Reactivity: 0

Personal Protection: E

National Fire Protection Association (U.S.A.):

Health: 1

Flammability: 1

Reactivity: 0

Specific hazard:

Protective Equipment:

Gloves.

Lab coat.
Dust respirator. Be sure to use an approved/certified respirator or equivalent.
Safety glasses.

Section 16: Other Information

References: Not available.

Other Special Considerations: Not available.

Created: 10/10/2005 12:10 AM

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MATERIAL SAFETY DATA SHEET

TRIS BASE

SECTION 1 - MATERIAL IDENTIFICATION AND INFORMATION

MANUFACTURER'S NAME: GENOMIC SOLUTIONS, INC.
ADDRESS: 4355 VARSITY DR.
ANN ARBOR, MI 48108
TELEPHONE NUMBER: (734) 975-4800
US EMERGENCY PHONE: (800) 535-5053
INTERNATIONAL EMERGENCY PHONE: 1(352) 323-3500 (Call Collect)

CAS NUMBER: 77-86-1
RTECS NUMBER: TY2900000

SUBSTANCE: TRIS BASE

TRADE NAMES/SYNONYMS:

80-0077, TRIS BASE, 500G; 80-0160, TRIS BASE, 2500G; 2-AMINO-2- (HYDROXYMETHYL) -1,3-PROPANEDIOL; AMINOTRIMETHYLOLMETHANE; AMINOTRIS (HYDROXYMETHYL) METHANE; TRIMETHYLOLAMINOMETHANE; TRIS (BUFFERING AGENT); TRIS BUFFER; TRIS (HYDROXYMETHYL) METHANAMINE; TRIS (HYDROXYMETHYL) METHYLAMINE; TRIS (METHYLOLAMINO) METHANE; TROMETHAMINE; TROMETHANE; TROMETHANMIN; TRISAMINE; TRIS (HYDROXYMETHYL) AMINOMETHANE; 1,3-PROPANEDIOL, 2-AMINO-2- (HYDROXYMETHYL) -; TRIS (HYDROXYMETHYL) AMINOMETHANE; C4H11NO3.

CHEMICAL FAMILY: AMINE, HYDROXYL, ALIPHATIC

CREATION DATE: 6/14/95
REVISED: 2/20/98

SECTION 2 - PHYSICAL / CHEMICAL CHARACTERISTICS

COMPONENT: TRIS(HYDROXYMETHYL)AMINOMETHANE
CAS NUMBER: 77-86-1
PERCENTAGE: 100
OTHER CONTAMINANTS: NONE

PHYSICAL AND CHEMICAL PROPERTIES

DESCRIPTION: Odorless, hygroscopic, crystalline mass or white crystalline powder
MOLECULAR WEIGHT: 121.14
MOLECULAR FORMULA: (H-O-C-H₂)₃-C-N-H₂
MELTING POINT: 340-342 F (171-172 C)
BOILING POINT: 426-428 F (219-220 C) @ 10 mmHg
VAPOR PRESSURE: no data available
VAPOR DENSITY: N/A
SPECIFIC GRAVITY: not available
WATER SOLUBILITY: 55%
VOLATILITY:
pH: 10.4 @ 1.2% solution
ODOR THRESHOLD: no data available
EVAPORATION RATE: N/A

MATERIAL SAFETY DATA SHEET

TRIS BASE

SOLVENT SOLUBILITY: Moderately soluble in methanol, ethanol, ethylene glycol, dimethylformamide; slightly soluble in acetone, ether; very slightly soluble in ethyl acetate, cyclohexane, chloroform, carbon tetrachloride.

SECTION 3 - FIRE AND EXPLOSION HAZARD DATA

CERCLA RATINGS (SCALE 0-3): HEALTH = 2 FIRE = 1 REACTIVITY = 0 PERSISTENCE = 0

NFPA RATINGS (SCALE 0-4): HEALTH = 2 FIRE = 1 REACTIVITY = 0

EMERGENCY OVERVIEW:

Odorless, hygroscopic, crystalline mass or white crystalline powder. Causes respiratory tract, skin and eye irritation. Avoid breathing dust. Avoid contact with eyes, skin and clothing. Keep container tightly closed. Wash thoroughly after handling. Use only with adequate ventilation.

POTENTIAL HEALTH EFFECTS

INHALATION:

Short Term Effects: May cause irritation. Additional effects may include coughing, chest pain and difficulty breathing.

Long Term Effects: No information is available.

SKIN CONTACT:

Short Term Effects: May cause irritation.

Long Term Effects: Same effects as short term exposure.

EYE CONTACT:

Short Term Effects: May cause irritation. Additional effects may include eye damage.

Long Term Effects: Same effects as short term exposure.

INGESTION:

Short Term Effects: May cause gastrointestinal irritation. Additional effects may include burns, digestive disorders and weakness.

Long Term Effects: No information is available.

CARCINOGEN STATUS:

OSHA: N

NTP: N

IARC: N

FIRE FIGHTING MEASURES

FIRE AND EXPLOSION HAZARD:

Slight fire hazard when exposed to heat or flame.

EXTINGUISHING MEDIA:

Dry chemical, carbon dioxide, water spray or regular foam (1993 Emergency Response Guidebook, RSPA P 5800.6).

For larger fires, use water spray, fog or regular foam (1993 Emergency Response Guidebook, RSPA P 5800.6).

FIREFIGHTING:

Move container from fire area if you can do it without risk. Do not scatter spilled material with high-pressure water streams. Dike fire-control water for later disposal (1993 Emergency Response Guidebook, RSPA P 5800.6, Guide Page 31).

Use agents suitable for type of surrounding fire. Avoid breathing hazardous vapors, keep upwind.

MATERIAL SAFETY DATA SHEET

TRIS BASE

FLASH POINT: no data available
LOWER FLAMMABLE LIMIT: no data available
UPPER FLAMMABLE LIMIT: no data available
AUTOIGNITION: no data available

HAZARDOUS COMBUSTION PRODUCTS:

Thermal decomposition products may include toxic oxides of carbon and nitrogen.

SECTION 4 - REACTIVITY HAZARD DATA

STABILITY AND REACTIVITY

REACTIVITY:

Stable under normal temperatures and pressures.

CONDITIONS TO AVOID:

May burn but does not ignite readily. Avoid contact with strong oxidizers, excessive heat, sparks, or open flame.

INCOMPATIBILITIES:

TRIS(HYDROXYMETHYL)AMINOMETHANE:

ACIDS: Vigorous reaction
ALKALIES (STRONG): Incompatible
ALUMINUM: Corrosive
BRASS: Corrosive
COPPER: Corrosive
OXIDIZERS (STRONG): Fire and explosion hazard

HAZARDOUS DECOMPOSITION:

Thermal decomposition products may include toxic oxides of carbon and nitrogen.

POLYMERIZATION:

Hazardous polymerization has not been reported to occur under normal temperatures and pressures.

SECTION 5 - HEALTH HAZARD DATA

EMERGENCY FIRST AID

INHALATION:

First Aid - Remove from exposure area to fresh air immediately. Perform artificial respiration if necessary. Keep person warm and at rest. Treat symptomatically and supportively. Get medical attention immediately.

SKIN CONTACT:

First Aid - Remove contaminated clothing and shoes immediately. Wash with soap or mild detergent and large amounts of water until no evidence of chemical remains (at least 15-20 minutes). Get medical attention immediately.

EYE CONTACT:

First Aid - Wash eyes immediately with large amounts of water or normal saline, occasionally lifting upper and lower lids, until no evidence of chemical remains (at least 15-20 minutes). Get medical attention immediately.

MATERIAL SAFETY DATA SHEET

TRIS BASE

INGESTION:

First Aid - If vomiting occurs, keep head lower than hips to help prevent aspiration. Treat symptomatically and supportively. Get medical attention if needed.

NOTE TO PHYSICIAN

ANTIDOTE: No specific antidote. Treat symptomatically and supportively.

TOXICOLOGY INFORMATION

TRIS(HYDROXYMETHYL)AMINOMETHANE:

TOXICITY DATA:

5900 mg/kg oral-rat LD50

1800 mg/kg intravenous-rat LD50

1000 mg/kg oral-rabbit LDLo

1210 mg/kg intravenous-mouse LD50

CARCINOGEN STATUS: None

LOCAL EFFECTS: Irritant- inhalation, skin, eye

ACUTE TOXICITY LEVEL: Slightly toxic by ingestion

TARGET EFFECTS: No data available

HEALTH EFFECTS

INHALATION:

TRIS(HYDROXYMETHYL)AMINOMETHANE:

IRRITANT.

Acute Exposure: May cause irritation of the mucous membranes with tightness and pain in the chest, coughing, and difficulty breathing.

Chronic Exposure: No data available.

SKIN CONTACT:

TRIS(HYDROXYMETHYL)AMINOMETHANE:

IRRITANT.

Acute Exposure: May cause irritation with redness, pain, and possibly sensitization.

Chronic Exposure: May cause dermatitis due to irritation or sensitization.

EYE CONTACT:

TRIS(HYDROXYMETHYL)AMINOMETHANE:

IRRITANT.

Acute Exposure: May cause irritation with redness, pain, and possibly corneal damage.

Chronic Exposure: Prolonged or repeated exposure to irritants may cause conjunctivitis.

INGESTION:

TRIS(HYDROXYMETHYL)AMINOMETHANE:

Acute Exposure: May cause gastrointestinal irritation and possibly burns to the mouth and stomach. Large doses to laboratory animals caused weakness, collapse and death. The estimated fatal dose is 50 grams.

Chronic Exposure: No data available.

SECTION 6 - CONTROL AND PROTECTIVE MEASURES

EXPOSURE LIMITS:

No occupational exposure limits established by OSHA, ACGIH, or NIOSH.

MATERIAL SAFETY DATA SHEET

TRIS BASE

VENTILATION:

Provide local exhaust ventilation. Ventilation equipment should be explosion-proof if explosive concentrations of dust, vapor or fume are present.

EYE PROTECTION:

Employee must wear splash-proof or dust-resistant safety goggles to prevent contact with this substance.

EMERGENCY WASH FACILITIES:

Where there is any possibility that an employee's eyes and/or skin may be exposed to this substance, the employer should provide an eye wash fountain and quick drench shower within the immediate work area for emergency use.

CLOTHING:

Employee must wear appropriate protective (impervious) clothing and equipment to prevent repeated or prolonged skin contact with this substance.

GLOVES:

Employee must wear appropriate protective gloves to prevent contact with this substance.

RESPIRATOR:

The following respirators are recommended based on information found in the physical data, toxicity and health effects sections. They are ranked in order from minimum to maximum respiratory protection.

The specific respirator selected must be based on contamination levels found in the work place, must be based on the specific operation, must not exceed the working limits of the respirator and must be jointly approved by the National Institute for Occupational Safety and Health and the Mine Safety and Health Administration (NIOSH-MSHA).

Any dust and mist respirator.

Any air-purifying respirator with a high-efficiency particulate filter.

Any powered air-purifying respirator with a dust and mist filter.

Any powered air-purifying respirator with a high-efficiency particulate filter.

Any type 'C' supplied-air respirator operated in the pressure-demand or other positive pressure or continuous-flow mode.

Any self-contained breathing apparatus.

FOR FIREFIGHTING AND OTHER IMMEDIATELY DANGEROUS TO LIFE OR HEALTH CONDITIONS:

Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode.

Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode.

SECTION 7 - PRECAUTIONS FOR SAFE HANDLING & USE/LEAK PROCEDURES

ACCIDENTAL RELEASE MEASURES

OCCUPATIONAL SPILL:

MATERIAL SAFETY DATA SHEET

TRIS BASE

Sweep up and place in suitable clean, dry containers for reclamation or later disposal. Do not flush spilled material into sewer. Keep unnecessary people away.

HANDLING AND STORAGE

Observe all federal, state and local regulations when storing this substance. Store away from incompatible substances. Store in a cool, dry place; keep container tightly closed when not in use.

DISPOSAL INFORMATION

Observe all federal, state and local regulations when disposing of this substance.

SECTION 8 - TRANSPORTATION AND REGULATORY INFORMATION
--

TRANSPORTATION INFORMATION:

No classification currently assigned

REGULATORY INFORMATION:

TSCA STATUS:	Y
CERCLA SECTION 103 (40CFR302.4):	N
SARA SECTION 302 (40CFR355.30):	N
SARA SECTION 304 (40CFR355.40):	N
SARA SECTION 313 (40CFR372..65):	N
OSHA PROCESS SAFETY (29CFR1910.119):	N
CALIFORNIA PROPOSITION 65:	N

SARA HAZARD CATEGORIES, SARA SECTIONS 311/312 (40 CFR 370.21)

ACUTE HAZARD:	Y
CHRONIC HAZARD:	N
FIRE HAZARD:	N
REACTIVITY HAZARD:	N
SUDDEN RELEASE HAZARD:	N

MATERIAL SAFETY DATA SHEET

TRIS BASE

While the information and recommendations set forth herein are believed to be accurate as of the date hereof, ESA, Inc. makes no warranty with respect thereto and disclaims all liability from reliance thereon.

Appendix F – Vendor Specification Sheets

Vendor Equipment	Page
Nunc™ EasYFlask™	466
Nunc™ PETG Roller Bottles	468
Cole Parmer™ Low-Profile Bottle Roller	470
Thermo Scientific™ Precision Incubators	471
Sartorius Stedim Biotech™ BIOSTAT® Cultibag RM	483
Sartorius Stedim Biotech™ Sartopore® 2	491
Watson Marlow™ 800-series pumps	493
Watson Marlow™ Bioprene tubing	505
Abec™ Bioreactors	507
Sharpsville Container Jacketed Tanks	508
Alfa Laval™ BTAX 215 Centrifuge	510
Sartorius™ Sartocube® - Hydrosart® Ultrafilter Cassette	514
Sartorius™ Hydrosart® Ultrafiltration Cassettes	516
Sartorius™ Sartocon® 2 Plus Stainless Steel Holder	518
Sartorius™ Sartocon 2 Plus Benchtop Crossflow System	520
Pall Life Sciences™ MEMBRAPlan® DG(M)	522
GE Healthcare™ Chromaflow Columns	529
Amersham Biosciences™ nProtein A Sepharose 4 Fast Flow	537
Scilog® Intelligent BioProcessing Systems	541
HyClone® Labtainer™ System	543
Quality Bioresources, Inc. Distribution Vials	545
Sani-Matic® CIP Washers	546
BioProfile® FLEX Cell Culture Analyzer	550
StarLIMS® Version 10	551



EasYFlask™ Family

225 cm²
New to the
Family!



For more information or samples, please call
1-800-446-2543 x7261 or
E-mail: cellculture@nunc.us

Complete product range

- Available in 25, 75, 175 and now 225 cm²

Ergonomic closure

- Easy open-and-close cap takes only 1/3 turn
- Distinctive "Y" shaped mark on the vent/close cap allows visual verification of the cap position

Low profile design

- Maximizes incubator space in the same footprint as conventional flasks
- Allows viewing of entire growth surface when estimating confluency using a standard microscope

Angled neck

- Large opening and angled neck allow for easy access to the entire growth surface with both pipettes and cell scrapers

Volume graduations

- Graduations are both printed and molded on the side wall of the flasks for easy use

Consistent performance

- Nunclon® Δ treated surface ensures optimal cell attachment and growth
- Certified non-pyrogenic and is tested for both monolayer formation and cloning efficiency employing primary cells as well as repeating cell lines

Maximum airflow

- Air flows under the flask to optimize temperature equilibration during incubation, even when stacked



Nunc EasYFlask – Nunclon Δ, radiation sterilized

Catalog Number	156340	156367	156472	156499	159920	159910	159933	159934
Culture area, cm ²	25	25	75	75	175	175	225	225
Closure	Vent/close	Filter	Vent/close	Filter	Vent/close	Filter	Vent/close	Filter
Cap Material	HDPE	HDPE	HDPE	HDPE	HDPE	HDPE	HDPE	HDPE
Sug. working volume, ml	7	7	25	25	55	55	70	70
Units per sleeve/case	10/200	10/200	5/100	5/100	5/30	5/30	5/30	5/30

Bulk closures for EasYFlask

Catalog Number	158892	158523	158240	157527	133002	133001
Closure	Vent/Close	Filter	Vent/Close	Filter	Vent/Close	Filter
Culture area, cm ²	25	25	75	75	175/225	175/225
Units per sleeve/case	1/100	1/100	1/100	1/100	1/100	1/100



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IN VITRO PETG Roller Bottles



InVitro Roller Bottles from Nalge Nunc International are available in surface areas from 1050 cm² to 4200 cm². All InVitro Roller Bottles are molded from PETG (polyethylene terephthalate G copolyester) and feature HDPE Quick-Action vented and non-vented ergonomic closures.

The patented* InVitro Expanded Surface (XPS) Roller Bottles greatly increase the capacity of existing roller apparatus without expanding your capital or labor costs.

*US Pat. Off. Nos. 4,824,787; 4,962,033 and 5,010,013

Features:

- Surface areas range from 1050 cm² to 4200 cm²
 - Fewer interventions, lower contamination risk
- Expanded Surface (XPS) Bottles have increased surface-to-volume ratios
 - Increases production without expanding facilities
- Molded of durable PETG
 - Stronger than glass under normal laboratory use
- Ergonomic vented and non-vented closures
 - Reduces wrist strain and increases productivity

Standard Roller Bottles - 1050 and 1800 cm²

The 1050 cm² 1.2X bottle is similar in overall size to standard 850 cm² bottles, but has 23% greater surface area for adherent or suspension cell cultures. It will accept approximately 800 ml of cell suspension in the horizontal position and is excellent for freezing to -40°C.

Twice as long as the 1.2X bottle, the 1800 cm² 1XL bottle reduces labor and sterile interventions by reducing the number of bottles required.

Expanded Surface Roller Bottles - 1700, 2100 and 4200 cm²

Patented* InVitro Expanded Surface (XPS) Roller Bottles provide up to 250% more growth area than same-volume standard bottles. XPS Bottles can conveniently expand existing production capacity and reduce interventions per bottle, resulting in lower risk of contamination.

InVitro XPS Roller Bottles have specially designed pleats that dramatically expand the available growth surface. The pleats are oriented in the direction of rotation to minimize turbulence. Flat panels between sections allow microscopic viewing and expedite drainage during medium replacement and cell harvest.

The 2X (1700 cm²) bottle's pleat profile provides faster drainage because of expanded pleats.

Both the 2.5X (2100 cm²) and 5X (4200 cm²) bottles have a shorter and tighter pleat design which allows for complete wetting of the surface with less volume.

Common Features

- Molded of durable PETG; an excellent substrate for adherent cell cultures
- Wide range of sizes; surface areas from 1050 cm² to 4200 cm²
- Expanded Surface (XPS) Bottles have improved surface-to-volume ratios for increased production without expanding facilities
- Ergonomic closure reduces wrist strain and increases productivity
- Vented closures available on the 1.2X standard size and as replacement closures
- Easy-to-read graduations for medium fills
- Lot number is printed on each bottle for traceability

*US Pat. Off. Nos. 4,824,787; 4,962,033 and 5,010,013

Cat. No.	Description	Closure type	Culture area, cm ²	Working volume, ml	Units sleeve/case
Standard Roller Bottles					
106005	1.2X PETG Roller Bottle	Standard	1050	100-500	5/20
106085	1.2X PETG Roller Bottle	Vent	1050	100-500	5/20
106020	1.2X PETG Roller Bottle	Standard	1050	100-500	20/20
186022	1XL PETG Roller Bottle	Standard	1800	200-1000	22/22

Expanded Surface (XPS) Roller Bottles					
176020	2X PETG Roller Bottle	Standard	1700	200-600	20/20
216005	2.5X PETG Roller Bottle	Standard	2100	200-600	5/20
216020	2.5X PETG Roller Bottle	Standard	2100	200-600	20/20
426022	5X PETG Roller Bottle	Standard	4200	400-1000	22/22

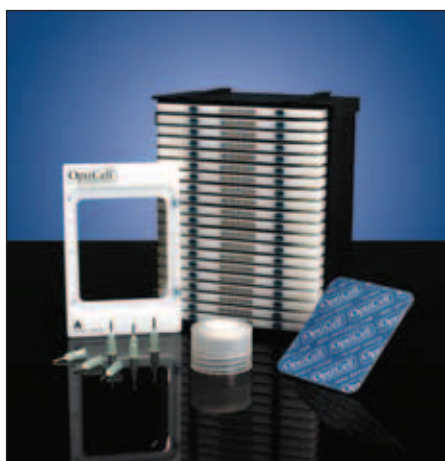
Replacement Closures					
308001	48 mm HDPE Vented Quick-Action Closure, Sterile				1/300



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OptiCell 1100 starter kit 01931-50



Resealing access ports provide closed growth environment.



36202-02

NUNC™ OptiCell™ Cell Culture System

New

Unique format for growing, monitoring, and transporting live cells

- Total growing area of 100 cm²
- Thin profile maximizes incubator space and reduces media consumption
- Barcoded for easy tracking and automation handling

System consists of two parallel gas-permeable, cell culture treated polystyrene membranes—2 mm apart—attached to a standard microtiter plate-sized frame. Two resealing access ports provide closed growth environment with a sterile fluid path to reduce the risk of contamination. Typical applications for these systems include transportation of live cells, hybridoma antibody production, biomagnetic cell separation, cell imaging and staining, and transfection.



Catalog number	Description	Contents	Price
R-01931-50	OptiCell 1100 starter kit	20 OptiCell 1100 chambers, 1 rack, 1 knife, 50 insertion tips, 2 caps, 1 optical shield, and 1 mini-CD	
R-01931-54	OptiCell MAX 2100 starter kit	5 OptiCell MAX 2100 chambers, 1 rack, 50 insertion tips, and hybridoma Ab production protocol	
R-01931-57	OptiMag cell separation kit	5 OptiCell 1100 chambers, 1 magnet, 50 insertion tips, 1 rack, and OptiMag cell separation protocol	
R-01931-59	OptiCell mailer kit	5 OptiCell 1100 chambers, 50 insertion tips, 5 OptiCell mailers, and shipping protocol	

Replacement Chambers

Catalog number	Description	Culture area/chamber	Working volume/chamber	Qty/cs	Price/cs
R-01931-51	OptiCell 1100	100 cm ²	10 mL	20	
R-01931-52				100	
R-01931-53				500	
R-01931-55	OptiCell 2100	100 cm ²	30 mL	20	
R-01931-56				100	

Accessories

R-01931-58 OptiMag cell separation magnet /ea
 R-01931-60 OptiCell mailer. Case of 10 /cs
 R-01931-61 OptiCell mailer. Case of 25 /cs

R-01931-62 OptiCell rack /ea
 R-01931-63 OptiCell insertion tips. Case of 100 /cs
 R-01931-64 OptiCell knife. Case of 3 /cs

Low-Profile Bottle Roller

Lightweight and portable—easy to transport from lab to lab

- Use from 0 to 60°C—operates in CO₂ and high humidity incubators
- Accommodates tubes from 10 mL up to 850 cm²

Use this low-profile bottle roller for growing bacteria and cell cultures. The low-profile shape saves benchtop and incubator shelf space. The thin, flat power cord reaches external outlets without damaging incubator gaskets. Adjust roller speed from 1 to 30 rpm. The unit comes with 6 rollers to accommodate tubes from 10 mL to 50 mL or up to three 850 cm² growth area culture bottles with a total of 1½ liters of liquid. The low-profile roller measures 15"L x 14¼"W x 2¾"H.

What's included: low-profile bottle roller, six rollers, and 6-ft power cord.

Catalog number	Power (50/60 Hz)	Price
R-36202-02	115 VAC	
R-36202-04	220 VAC	

R-36202-50 Additional bottle roller



Thermo Scientific Precision Incubators

Performance, Quality and Value for Your Incubation Needs

Global Leader in **Quality and Reliability**

For more than 50 years, Thermo Scientific products have been trusted by the world's leading biotechnology, pharmaceutical, academic, industrial and clinical laboratories. Our solutions deliver the performance, quality and reliability required by researchers and clinicians worldwide.



Thermo Scientific Precision Incubators

Our new Thermo Scientific Precision incubator series delivers excellent temperature uniformity, performance and value for a wide range of microbiological incubation applications – from everyday needs to demanding incubation and storage tasks.

Precision® High-Performance Incubators pg. 3-6

> Superior Temperature Uniformity

Precision Standard Incubators pg. 7

> For Everyday Incubation Applications

Precision Compact Incubators pg. 8

> Space-Saving Design for Basic Applications

Precision Refrigerated Incubators pg. 9-10

> For Various Applications at Temperatures Below and Above Ambient

APPLICATIONS	Precision High-Performance Incubators	Precision Standard Incubators	Precision Compact Incubators	Precision Refrigerated Incubators
Bacterial Research		•	•	•
Biochemical Oxygen Demand (BOD)				•
Chemical Storage	•	•		•
Chick Embryo Studies		•	•	
Coliform Determinations	•	•	•	•
Crystallization Studies	•	•		
Drying And Staining Procedures	•	•		•
Entomological Studies				•
Enzyme Digestion Studies	•	•		•
Hematological Testing	•	•	•	•
Microbiological Determinations	•	•	•	•
Paraffin Embedding	•	•		
Pharmaceutical Stability Testing	•			
Sample Storage	•			•
Tissue Culturing	•	•	•	•
Plant Growth Studies				•

Thermo Scientific Precision High-Performance Incubators

> Mechanical or Gravity Convection

Featuring advanced microprocessor controls, our Precision high-performance incubators are available with mechanical or gravity convection for your most important applications that require excellent temperature distribution or gentle sample incubation and handling between 5°C above ambient to 75°C.



Choice of Mechanical or Gravity Convection

- Mechanical convection provides uniform heating and precise temperature control. A blower circulates heated air in a horizontal airflow pattern for efficient heat distribution with tight temperature tolerances of up to $\pm 0.3^{\circ}\text{C}$
- Gravity convection offers safe incubation with reduced air changes, minimizing drying-out of samples while providing a stable environment

Advanced Microprocessor Controls

- Sophisticated microprocessor controls feature easy-to-view digital LED readout and reliable temperature control
- Fixed setpoints on control panel eliminate the need for tuning and off-set feature enables easy calibration
- Temperature is displayed on large, three-character screen and can be easily set from 5°C above ambient to 75°C in 0.1°C increments using touch-sensitive arrow keys

Built-In Safety

- Built-in safety back-up maintains control at 3°C above setpoint if primary heater control fails
- Visual alarm indicates when temperature exceeds 3°C setpoint
- Silicone gasket on outer door and 3" thick fiberglass insulation prevents heat loss and ensures excellent temperature uniformity
- Circuit breaker protects against power surges.

Simplicity and Flexibility

- Inner glass door permits viewing of samples without disturbing the chamber environment
- Internal electrical outlet allows operation of a shaker, stirrer or other lab apparatus

Durable and Robust

- Cabinet has durable, enamel-coated steel exterior. Interior chamber features easy-to-clean stainless steel
- Low-watt density heater elements are designed for long life and energy efficiency

Mechanical Convection Models

- Stackable, table-top units
- Outer door opens to 180° for unhindered access
- Double door unit and large capacity units also available
- Choice of 120V and 240V versions
- Internal electrical outlet in all models



High-Performance Mechanical Convection				Double Doors	Large Capacity
Chamber Volume	2.2 cu. ft./62 L	3.4 cu. ft./96 L	4.5 cu. ft. /127 L	11.2 cu. ft./317 L	30 cu. ft./850 L
Temperature Control	Microprocessor PID	Microprocessor PID	Microprocessor PID	Hydraulic Thermostat	Hydraulic Thermostat
Temperature Display	LED	LED	LED	LED	Thermometer
Temperature Range	ambient +5° to 75°C	ambient +5° to 75°C	ambient +5° to 75°C	ambient +5° to 65°C	ambient +5° to 70°C
Uniformity @37°C	±0.5°C	±0.5°C	±0.5°C	± 0.6°C	±0.5°C
Dimensions (W x H x D)					
Chamber	18 x 12.5 x 18 in.	18 x 19 x 18 in.	18 x 25.5 x 18 in.	37 x 25 x 21 in.	30 x 72 x 24.25 in.
	(46 x 32 x 46 cm)	(46 x 48 x 46 cm)	(46 x 65 x 46 cm)	(94 x 64 x 53 cm)	(72.2 x 182.9 x 61.6 cm)
Exterior	25 x 26 x 23.5 in.	25 x 33 x 23.5 in.	25 x 39 x 23.5 in.	39.8 x 34.5 x 25 in.	36 x 88.5 x 31.5 in.
	(64 x 66 x 60 cm)	(64 x 84 x 60 cm)	(64 x 99 x 60 cm)	(101 x 88 x 64 cm)	(91.4 x 224.5 x 74.3 cm)
Electrical Specs					
120 V (60Hz)	330 watts/8.3 amps	330 watts/8.3 amps	410 watts /8.9 amps	520 watts/4.3 amps	450 watts/12.1 amps
240 V (50/60Hz)	330 watts/6.6 amps	330 watts/6.6 amps	410 watts/7.0 amps	520 watts/2.2 amps	—
Shelves	1 supplied, 3 max	1 supplied, 6 max	2 supplied, 10 max	6 supplied, 36 max*	6 supplied, 30 max
Catalog Number					
120 V	PR205045M	PR205055M	PR205065M	PR205075M	3971, solid door 3973, glass door
240 V	PR205040M	PR205050M	PR205060M	PR205070M	
Shipping Weight	150 lb/68 kg	165 lb/74.5 kg	190 lb/86.2 kg	215 lb/98 kg	685 lb/310.7 kg

**18 shelves per door opening*

Additional shelf kits for table top units: Catalog Number 13247S

Additional shelf kits for double door units: Catalog Number AY2076X1

Additional shelf kits for large capacity units: Catalog Number 3166190

All 120V table top units are UL/cUL listed.

12 month warranty (parts and labor)





Gravity Convection Models

- *Three stackable, table-top units*
- *Outer door opens to 180° for unhindered access*
- *Choice of 120 V and 240 V versions*
- *Electrical outlet in all models*



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Thermo Scientific Precision High-Performance Incubators (continued)

High-Performance Gravity Convection				Double-Door
Chamber Volume	2.5 cu. ft./71 L	3.75 cu. ft./106 L	5 cu. ft./142 L	11.2 cu. ft./317 L
Temperature Control	Microprocessor PID	Microprocessor PID	Microprocessor PID	Microprocessor PID
Temperature Display	LED	LED	LED	LED
Temperature Range	ambient +5° to 75°C	ambient +5° to 75°C	ambient +5° to 75°C	ambient +5° to 65°C
Uniformity @37°C	±0.7°C	±0.7°C	±0.7°C	±0.4°C
Sensitivity	±0.1°C	±0.1°C	±0.1°C	±0.2°C
Dimensions (W x H x D)				
Chamber	18 x 13.5 x 18 in.	18 x 20 x 18 in.	18 x 26.5 x 18 in.	37 x 25 x 21 in.
	(46 x 34 x 46 cm)	(46 x 51 x 46 cm)	(46 x 67 x 46 cm)	(94 x 64 x 53 cm)
Exterior	25 x 26 x 23.5 in.	25 x 33 x 23.5 in.	25 x 39 x 23.5 in.	40 x 35 x 25 in.
	(64 x 66 x 60 cm)	(64 x 84 x 60 cm)	(64 x 99 x 60 cm)	(101 x 88 x 64 cm)
Electrical Specs (50/60Hz)				
120 V (60Hz)	260 watts/2.2 amps	260 watts/2.2 amps	320 watts/2.7 amps	450 watts/3.8 amps
240 V (50/60Hz)	260 watts/1.1 amps	260 watts/1.1 amps	320 watts/1.4 amps	450 watts/1.9 amps
Shelves	1 supplied, 5 max	1 supplied, 8 max	2 supplied, 11 max	6 supplied, 36 max*
Catalog Number				
120 V	PR205045G	PR205055G	PR205065G	PR205075G
240 V	PR205040G	PR205050G	PR205060G	PR205070G
Shipping Weight	115 lb/ 52 kg	130 lb/59 kg	145 lb/66 kg	215 lb/98 kg

* 18 shelves per door opening

Additional shelf kits for table top units: Catalog Number 13247S

Additional shelf kits for double door units: Catalog Number AY2076X1

All table top units (120 V and 240 V) are UL/cUL listed.

12 month warranty (parts and labor)



Thermo Scientific Precision Standard Incubators



Economy and Value

Our Precision standard incubators are ideal for everyday applications that require temperatures between 5°C above ambient to 65°C and feature gravity convection for uniform heat distribution and reduced air movement to protect samples from drying out.



Uniform Temperature Protects Samples

- Gravity convection permits heat to enter from all points on the wall and floor of incubator for uniform heat distribution and reduced air movement to prevent drying out
- Adjustable hydraulic thermostat ensures stable temperature throughout chamber
- Superior heat distribution eliminates hot spots and provides temperature uniformity of up to $\pm 1^{\circ}\text{C}$ at 37°C

Excellent Safety

- Radiant wall heaters outside chamber eliminate safety hazards of exposed heaters
- Environmentally friendly, mercury-free thermometer included
- Pilot light indicates when heaters are energized for safe operation

Durability and Easy Cleaning

- Corrosion-resistant aluminum chamber is easy to clean
- Powder-coated exterior steel construction ensures durability
- Shelves are perforated for optimized temperature transfer to samples and can easily be removed for thorough cleaning

Standard Incubators

Chamber Volume	1.3 cu. ft. /37 L	5.1 cu. ft. /144 L
Temperature Control	Hydraulic Thermostat	Hydraulic Thermostat
Temperature Display	Thermometer	Thermometer
Temperature Range	ambient +5° to 65°C	ambient +5° to 65°C
Uniformity @37°C	$\pm 1^{\circ}\text{C}$	$\pm 1.3^{\circ}\text{C}$
Dimensions (W x H x D)		
Chamber	13 x 13 x 13 in. (33 x 33 x 33 cm)	18 x 27 x 18 in. (46 x 69 x 46 cm)
Exterior	15.7 x 21 x 15 in. (40 x 53 x 38 cm)	21 x 33 x 21 in. (53 x 84 x 53 cm)
Electrical Specs		
120 V (60Hz)	200 watts/1.7 amps	400 watts/3.3 amps
240 V (50/60Hz)	200 watts/0.8 amps	400 watts/1.7 amps
Shelves	2 supplied, 5 max	2 supplied, 9 max
Catalog Numbers		
120 V	PR205125G	PR205165G
240 V	PR205120G	PR205160G
Shipping Weight	51 lb/23 kg	94 lb/41 kg

Two Chamber Sizes

- 1.3 cu. ft. (37L) includes two adjustable aluminum shelves
- 5.1 cu. ft. (144L) includes two adjustable aluminum shelves

(*Additional shelves are sold separately)

Additional shelf kits for the 1.3 cu. ft. models:
Catalog Number 203-8Q

Additional shelf kits for the 5.1 cu. ft. models:
Catalog Number 403-8Q

All 120V units are UL/cUL listed.
12 month warranty (parts and labor)

Thermo Scientific Precision Compact Incubators

Space-Saving Design

Featuring a space-savings footprint for maximizing workspace, our Precision compact incubators are ideal for small clinics and laboratories that require temperatures between 5°C above ambient to 40°C or 60°C for basic applications.

Space-Efficient Design

- Small footprint saves valuable bench space

Temperature Uniformity

- Easily adjustable bi-metallic thermostat controls and aluminum chamber ensure excellent temperature uniformity
- Rugged metal door with positive latch provides excellent seal for temperature stability
- 1" thick fiberglass insulation prevents heat loss (0.67 cu. ft. and 1.0 cu. ft. units only)

Safe Operation

- Shielded heating elements eliminate safety hazards caused by spills
- Pilot light indicates when heaters are energized for safe operation
- Environmentally, mercury-free thermometer included

Durability and Easy Cleaning

- Corrosion-resistant aluminum chamber is easy to clean
- Powder-coated paint and exterior steel construction ensure durability



Compact Incubators

Chamber Volume	0.67 cu. ft./19 L	1 cu. ft./28	1.32 cu. ft./37 L
Temperature Control	Bimetallic Thermostat	Bimetallic Thermostat	Bimetallic Thermostat
Temperature Display	Thermometer	Thermometer	Thermometer
Temperature Range	ambient +5° to 40°C	ambient +5° to 60°C	ambient +5° to 45°C
Uniformity @37°C	±1°C	±1°C	±3°C
Dimensions (W x H x D)			
Chamber	12 x 8 x 12 in. (30 x 20 x 30 cm)	12 x 12 x 12 in. (30 x 30 x 30 cm)	13.44 x 12.68 x 12.65 in. (35 x 32 x 35 cm)
Exterior	13.5 x 11.8 x 14.5 in. (34 x 30 x 37 cm)	13.5 x 15.7 x 13.9 in. (34 x 40 x 35 cm)	13.5 x 15.7 x 13.9 in. (37 x 40 x 35 cm)
Electrical Specs (50/60Hz)			
120 V	100 watts/0.8 amps	100 watts/0.8 amps	150 watts/1.3 amps
240 V	100 watts/0.4 amps	100 watts/0.4 amps	150 watts/0.6 amps
Shelves	1 supplied, 1 max	1 supplied, 1 max	2 supplied, 2 max
Catalog Numbers			
120 V	PR205215G	PR205225G	PR205235G
240 V	PR205210G	PR205220G	PR205230G
Shipping Weight	15 lb/7 kg	27 lb/12 kg	-479- 33 lb/15 kg

Three Convenient Sizes

- 0.67 cu. ft. (19L) includes thermometer and one fixed shelf
- 1 cu. ft. (28L) includes thermometer and one removable shelf
- 1.32 cu. ft (37L) includes thermometer and two fixed shelves*

* Unit comes with plexiglass door for unobstructed viewing. For egg incubation, not for clinical use, microbiological or biochemical studies.

All 120V units are UL/cUL listed.
12 month warranty (parts and labor)

Thermo Scientific Precision Refrigerated Incubators



Broad Temperature Range

Featuring microprocessor controls and forced air circulation, our Precision refrigerated incubators are ideal for applications that require temperatures ranging from -15°C to 60°C with excellent stability.



Model 818



Model 815

Efficient, Dependable Design

- Easy-to-clean, corrosion resistant construction
- Compressor relay conserves energy
- 2A outlet easily supports apparatus inside the unit

Excellent Temperature Uniformity

- Microprocessor control with easy-to-read display shows actual temperature within 0.1°C
- Push-button controls feature temperature set-point selection
- Forced air circulation delivers excellent temperature stability
- CFC-free, foamed polyurethane insulation prevents heat loss
- RTD temperature probe and protected setpoint mode prevent accidental temperature change
- Door key lock protects samples from unauthorized access

20 cu. ft. Model 815 Refrigerated Incubator:

- Ideal for BOD applications and temperature settings at or below ambient
- Advanced microprocessor controlled with easy-to-use push buttons and set-points
- Connection for external chart recorder and RS-232 interface for data logging
- Holds up to 333 BOD bottles (300 ml)



Refrigerated Incubators			Model 815	Model 818/Plant Growth
Chamber Volume	6.1 cu. ft./173 L	30.4 cu. ft./861 L	20 cu. ft./566 L	17.8 cu. ft./504 L
Temperature Control	Microprocessor Controlled	Microprocessor Controlled	Microprocessor Controlled	Microprocessor Controlled
Temperature Display	LED	LED	LED	LED
Temperature Range	-10°C to +60°C	-15 C to 50 C	-10°C to +50°C	-10°C to +50°C / +10°C to +50°C*
Uniformity @37°C	±1.0°C	±1.0°C	±0.5°C	±1.5°C @ 20°C
Sensitivity @37°C	±0.1°C	±0.1°C	±0.1°C	±0.2°C
Dimensions (W x H x D)				
Chamber	20.5 x 28 x 20.5 in. (52 x 53 x 70 cm)	32 x 65.6 x 25 in. (81 x 166 x 64 cm)	26.5 x 57 x 20 in. (67.3 x 144.8 x 50.8 cm)	26.5 x 57 x 20 in. (67.3 x 144.8 x 50.8 cm)
Exterior	24 x 34.5 x 24.5 in (61 x 88 x 62 cm)	35 x 74 x 33 in. (89 x 188 x 84 cm)	32 x 75 x 29 in. (82 x 191 x 74 cm)	32 x 75 x 29 in. (82 x 191 x 74 cm)
Electrical Specs				
115 V	860 watts/9.5 amps	1600 watts/16 amps	800 watts/ 7.0 amps	860 watts/7.5 amps
230 V	860 watts/5.8 amps	1600 watt/9 amps	800 watts/3.5 amps	860 watts/3.75 amps
Shelves	2 supplied, 4 max	4 supplied, 7 max	6 supplied, 6 max	6 supplied, 6 max
Catalog Number				
115 V	PR205745R	PR205795R	3721	3759
230 V	PR205740R	PR205790R	3722	3758
Shipping Weight	126 lb/57 kg	360 lb/163 kg	315 lb/142.9 kg	347 lb/157.4 kg

All 115V units are cCSAus listed.

* with illumination

12 month warranty (parts and labor)

17.8 cu. ft. Model 818 Plant Growth Chamber:

- Ideal for applications requiring night/day simulation, precise temperature control and uniformity over a broad temperature range
- Dual-lamp fluorescent lighting provides 300 foot candles for uniform illumination
- Programmable heating and lighting cycles: 7-day program with 2 light cycles per day





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biotech

BIOSTAT® CultiBag RM Culturing Convenience



turning science into solutions

Culturing Convenience

The BIOSTAT® CultiBag RM is the new generation of disposable bioreactors utilizing rocking motion for mixing with low shear. The combination of a new generation of Sartorius Stedim Biotech engineered control capabilities launches the disposable bioreactor system into a new era of cultivation. The disposable cultivation chamber CultiBag RM is specially designed for shear sensitive cells and any single-use applications. A comprehensive validation and extractables report is available for the bags and can also be designed for your process.

Maintenance and overhead expenses are reduced, eliminating the need for:

- Sterilization in Place (SIP)
- Cleaning In Place (CIP)
- Reduction in WFI
- Reduction in user time | effort
- Reduction in validation requirements

The measurement and control capabilities supplied by Sartorius Stedim Biotech are second to none. Utilizing proven technology and expert engineering, we have developed our existing in-house systems to bring powerful control capabilities to the disposable market. The BIOSTAT® RM Control Tower presents an easy-to-use touch screen control with integrated measurement and control hardware, pumps, temperature and gassing systems, for excellent process control.

The application-driven, configured packages for basic, optical and perfusion provide everything needed to get started immediately. The BIOSTAT® CultiBag RM is available in scalable working volumes from 0.1 L to 100 L. Just select the size that meets your needs today. Each basic, optical and perfusion package also includes our BioPAT® MFCS/DA data logging software. A large variety of operation modes facilitates a batch-oriented bioprocessing.

Technical Specifications

	Dimensions W × H × D (mm)	Weight (kg)
BIOSTAT® RM Control Tower	320 × 735 × 565 mm	60 kg
Rocker 2 with Holder 2	330 × 400 × 430 mm	7 kg
Rocker 2 with Holder 10	550 × 200 × 430 mm	8 kg
Rocker 20/50 with Holder 20	710 × 400 × 560 mm	27 kg
Rocker 20/50 with Holder 50	1030 × 450 × 580 mm	32 kg
200 L Optical System	1998 × 1241 × 830 mm	272 kg

Utilities

Power supply	120 VAC and 230 VAC 208 VAC and 400 VAC
--------------	--



**The BIOSTAT® CultuBag RM
is ideal for**

- Cell culture, growth of animal, insect and plant cells
- Shear sensitive cells or anaerobic bacteria
- Transition from shake or tissue culture flasks
- Seed Cultivation for large scale Bioreactors
- Production scale up to 100 L
- For all your disposable applications





The BIOSTAT® CultiBag RM packages are specially configured to meet your disposable needs



Basic Packages –

Used for simple and easy cultivations. The rocker is used as a standalone unit with the heater blanket for temperature control and is equipped with an integrated air pump and flow controller for bag inflation and supply to cells. Alternatively the unit may be placed inside an incubator for temperature control and air supply to the cells. Additionally, a pressure relief valve and flow controller are included for attachment to your own gas mixing device. Rocking rate and rocking angle can be adjusted individually.



Optical Packages –

Designed for batch and fed-batch processes. Process control is achieved through disposable optical chemical pH and DO sensors. Feedback control of both values is available for your process. Two integrated pumps are included.



Perfusion Packages –

Designed for continuous cultivation. Two additional integrated pumps are supplied for feed| harvest control by weight. Balances are included for excellent perfusion control.



BioPAT® MFCS/DA

All packages are equipped with BioPAT® MFCS/DA software for external data logging. All batch related data can be stored in an individual folder allowing batch-oriented bioprocessing. Its plotting module together with the integrated export function to MS Excel is both user friendly and highly flexible.

Packages



Disposable optical chemical pH and DO sensors assure total process control in your application



An easy to use touch screen interface makes the operation of your BIOSTAT® CultiBag RM system very convenient and keeps training to a minimum

Basic Packages

- Standalone Unit
- Rocker only
- Integrated pump or external aeration module for inflation of bag and supply of ambient air to the cells
- Pressure relief and flow controller for connection to an external gas supply device
- Rocking angle and rocking rate control
- Temperature control heater blanket included
- Rocker may alternatively be placed into a CO₂ incubator
- BioPAT® MFCS/DA data logging software included

Optical Packages

- Standalone Unit
- Rocker with Optical Control Tower

Optical Tower

- Disposable optical chemical pH and DO sensors are included
- Feedback control of pH
- Feedback control of DO
- Intuitive touchscreen
- Trend display
- 2 integrated pumps
- Pressure control for overpressure safety
- Gassing by 4 × rotameters and 2 × mass flow controllers to overlay aeration
- BioPAT® MFCS/DA data logging software included

Perfusion Packages

- Standalone Unit
- Rocker with Perfusion Control Tower

Perfusion Tower

- Balances for feed | harvest flow control are included
- Disposable optical chemical pH and DO sensors are included
- Feedback control of pH
- Feedback control of DO
- Intuitive touchscreen
- Trend display
- 4 integrated pumps
- Pressure control for overpressure safety
- Gassing by 4 × rotameters and 2 × mass flow controllers to overlay aeration
- BioPAT® MFCS/DA data logging software included

Bag Designs

Basic Bags*

- Air inlet | air outlet filter
- Sample port
- Fill | drain and spare ports
- Female luer, female MPC or male MPC connectors
- Ports with dip tubes

Optical Bags*

- Air inlet | air outlet filter
- Sample port
- Fill | drain and spare ports
- Female luer, female MPC or male MPC connectors
- Ports with dip tubes
- Optical chemical DO sensor
- Optical chemical pH sensor

Perfusion Pro Bags*

- Air inlet | air outlet filter
- Sample port
- Fill | drain and spare ports
- Female luer, female MPC or male MPC connectors
- Ports with dip tubes
- Optical chemical DO sensor
- Optical chemical pH sensor
- Feed | harvest ports
- Acid | base port
- Internal fixed perfusion membrane



The needleless Septum port in all standard CultiBags RM facilitates your sampling process and keeps it safe at all times.

Customized bags also available

* Bags not included in packages

Hardware Technical Specifications



Description	Rockers and Controllers		
	Rocker 2	Rocker 20/50	Rocker 200
Bag Sizes	1 L, 2 L, 10 L	2 L, 10 L, 20 L, 50 L	100 L, 200 L
Power Supply			
120 VAC 208 VAC*	•	•	•
230 VAC 400 VAC*	•	•	•
Rocker Includes			
Air Pump	•	•	•
Pressure Regulator	•	•	•
Rocking Angle (degrees)	5–10	5–10	4–10
Rocking Rate (rocks/min)	6–42	8–42	3–20
Basic Package			
	Rocker only	Rocker only	n/a
Heater Plate	•	•	–
Bag Holder	•	•	–
Filter Heater	•	•	–
Tinted Lid	•	•	–
Control Tower	–	–	–
BioPAT® MFCS/DA	•	•	–
Optical Package			
	n/a	Rocker + Optical Control Tower	Rocker + Optical Control Tower
Heater Plate	–	•	•
Optical Control Tower	–	•	•
Rotameter for air, O ₂ , N ₂ , CO ₂	–	•	•
MFC for Total Flow	–	•	•
MFC for CO ₂	–	•	•
Temperature Control (°C)	–	20–40	20–40
pH Control	–	5.5–9	5.5–9
DO Control	–	0–100 %	0–100 %
Cascade Control on Controller	–	•	•
Aeration Module on Controller	–	•	•
Peristaltic pumps (integrated)	–	2	2
BioPAT® MFCS/DA	–	•	•
Perfusion Package			
	n/a	Rocker + Perfusion Control Tower	Rocker + Perfusion Control Tower
In addition to Optical Package:			
Peristaltic pumps	–	2	2 per side
Balances	–	2	2 per side

For additional information and order codes please refer to our datasheets BIOSTAT® CultiBag RM 2, BIOSTAT® CultiBag RM 20/50 and BIOSTAT® CultiBag RM 200.

• or value = included

– = not included

* Rocker 200 only

Bag Technical Specifications

Description	Standard Bags						
Sizes							
CultiBag Basic	1L	2L	10L	20L	50L	100L	200L
CultiBag Optical	–	2L	10L	20L	50L	100L	200L
CultiBag Perfusion Pro	–	2L	10L	20L	50L	100L	200L
Total Volume (L)	1	2	10	20	50	100	200
Min Working Volume (L)	0.1*	0.2*	1*	2*	5*	10*	20*
Max Working Volume (L)	0.5	1	5	10	25	50	100
Fittings (ID x OD)							
Air Inlet Filter	1	1	1	1	1	2	2
Air Outlet Filter	1	1	1	1	1	1	1
Sample port	1	1	1	1	1	2	2
Female Luer, C-Flex 1/8" x 1/4", dip tube	1	1	–	–	–	–	–
	–	1	–	–	–	–	–
	–	–	–	–	–	–	–
Female Luer, C-Flex 1/8" x 1/4"	–	–	1	1	1	1	1
	–	–	1	1	1	1	1
	–	1	1	1	1	1	1
Female Luer, Silicone 3/16" x 5/16"	1	2	1	2	2	2	2
	–	2	1	1	1	1	1
	–	1	–	–	–	–	–
Female MPC, C-Flex 1/4" x 7/16", dip tube	–	–	1	1	1	–	–
Male MPC, C-Flex 1/4" x 7/16"	–	–	–	–	1	–	–
Male MPC, C-Flex 3/8"x5/8"	–	–	–	–	–	1	1
Male MPC, C-Flex 3/8" x 5/8", dip tube	–	–	–	–	–	1	1
pH and DO optical chemical sensor	–	–	–	–	–	–	–
	–	•	•	•	•	•	•
	–	•	•	•	•	•	•
Fittings CultiBag RM Perfusion Pro only:							
Perfusion membrane 1.2 µm	–	•	•	•	•	•	•
Perfusion membrane 5 µm	–	•	•	•	•	•	•
Female Luer, Pharmed 1/16" x 3/16", C-Flex 1/8" x 1/4", dip tube	–	1	1	–	–	–	–
Female Luer, Pharmed 1/16" x 3/16", C-Flex 1/8" x 1/4"	–	1	1	–	–	–	–
Female Luer, Pharmed 1/8" x 1/4", C-Flex 1/8" x 1/4", dip tube	–	–	–	1	1	–	–
Female Luer, Pharmed 1/8" x 1/4", C-Flex 1/8" x 1/4"	–	–	–	1	1	–	–
Female Luer, Pharmed 3/16" x 5/16", C-Flex 1/4" x 7/16", dip tube	–	–	–	–	–	1	1
Female Luer, Pharmed 3/16" x 5/16", C-Flex 1/4" x 7/16"	–	–	–	–	–	1	1



- or number = included
- = not included
- = applies to all Bag types
- = applies to basic Bags only
- = applies to optical Bags only
- = applies to perfusion Bags only

* Bags with sensors require a higher minimum working volume than indicated

For additional information and order codes please refer to our datasheet CultiBag RM.

Sales and Service Contacts

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Sartopore® 2 0.2 µm

Sterilizing Grade Filter Cartridges



Description

Sartopore® 2 0.2 µm rated sterilizing grade filter cartridges are designed for filtration of a broad range of pharmaceutical products where compliance with cGMP requirements has to be fulfilled. Sartopore® 2 cartridges feature a unique hydrophilic heterogeneous double layer Polyethersulfone membrane with broad chemical compatibility, high thermal resistance and higher throughput and flow-rate than any other sterilizing grade filter cartridge.

Applications

Typical applications include sterilizing grade filtration of:

- Therapeutics
- Biological Fluids
- Ophthalmics
- SVPs, LVPs
- Antibiotics
- WFI
- Chemicals
- Cleaning and sanitizing agents
- Bulk pharmaceutical products

Compatibility

The polyethersulfone membrane is compatible with a pH range from pH 1 to pH 14 and unaffected by steam sterilization cycles making Sartopore® 2 cartridges ideal for filtration of solutions with high | low pH and for SIP | CIP-cycles.

Performance

Sartopore® 2 cartridges provide an exceptionally high total throughput by fractionated filtration due to the "built-in prefiltration" of the 0.45 µm membrane. The asymmetric pore structure of the polyethersulfone membrane provides high flow rates at low pressure drops.

Wettability

Sartopore® 2 cartridges can be easily wetted out for integrity testing even after drying at 80 °C for 12 hours.

Microbiological Retention

Sartopore® 2 filter cartridges are fully validated as sterilizing grade filter elements according to HIMA and ASTM F-838-83 guidelines.

Quality Control

Each individual element is integrity tested by diffusion and bubble point test prior to release, assuring absolute reliability.

Documentation

Sartopore® 2 cartridges are designed, developed and manufactured in accordance with an ISO 9001 certified Quality Management System. A Validation Guide and Extractables Guide are available for compliance with regulatory requirements.

Specifications

Materials of Construction

Prefilter Membrane:	Polyethersulfone, asymmetric
Endfilter Membrane:	Polyethersulfone, asymmetric
Support Fleece:	Polypropylene
Core:	Polypropylene
End Caps:	Polypropylene
O-Rings:	Silicone (optional EPDM or Viton)

Pore Size

0.45 µm + 0.2 µm

Available Sizes | Filtration Area

Size 1	10"	0.6 m ²	6 ft ²
Size 2	20"	1.2 m ²	12 ft ²
Size 3	30"	1.8 m ²	18 ft ²

Available Adapters | Connectors

21, 25, 27, 28

Operating Parameters

Max. Allowable Differential Pressure:	5 bar 75 psi at 20 °C
	2 bar 29 psi at 80 °C
Max. Allowable Back Pressure:	2 bar 29 psi at 20 °C

Specifications

Extractables

Sartopore® 2 0.2 µm rated filter cartridges meet, or exceed the requirements for WFI quality standards set by the current USP.

Regulatory Compliance

100% Individually integrity tested

Integrity test correlated to HIMA/ASTM F 838-83 Bacteria Challenge Test

Non-pyrogenic according to USP Bacterial Endotoxins

Passes USP Plastics Class VI Test

Non-fiber releasing according to 21 CFR

Sterilization

In-Line Steam Sterilization:

134 °C, 20 min. at max differential pressure of 0.5 bar | 7.25 psi

Autoclaving:

134 °C, 2 bar | 29 psi, 30 min

Sterilization Cycles

In-Line Sterilization: Min. 25
Autoclaving: Min. 25

Technical References

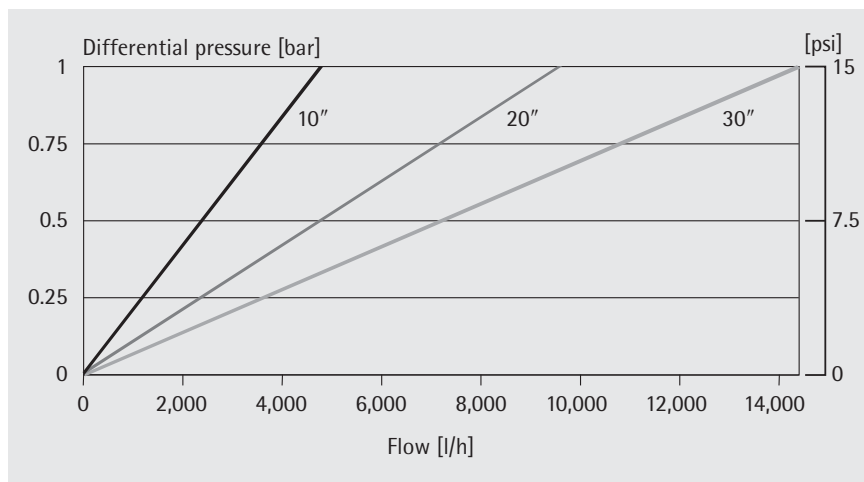
Validation Guide:

SPK 5732-e

Extractables Guide:

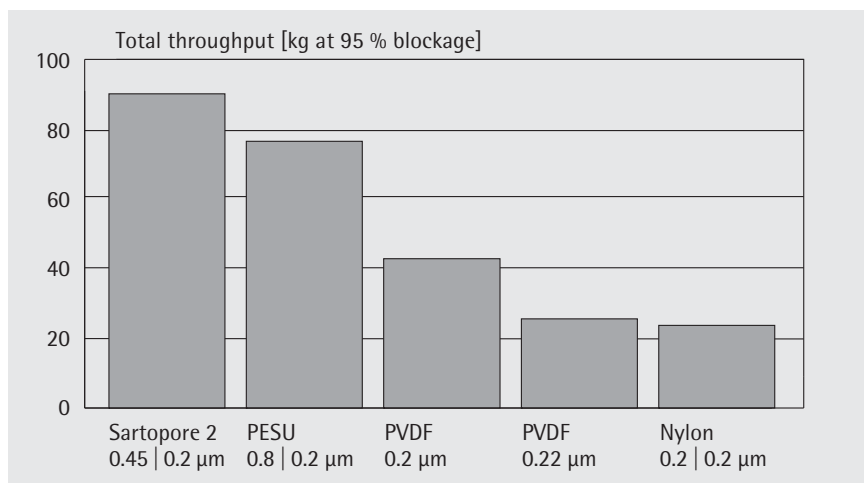
SPK 5731-e

Water Flow Rates for 10", 20" and 30" Cartridges



Standardized at 20 °C

Total Throughput Comparison



10" Cartridge format

Ordering Information

Order Code.	Pore size [µm]	Test Pressure [bar psi]	Max. Diffusion [ml/min]	Min. B.P. [bar psi]
544**07H1	0.2	2.5 36	18	3.2 46
544**07H2	0.2	2.5 36	36	3.2 46
544**07H3	0.2	2.5 36	54	3.2 46

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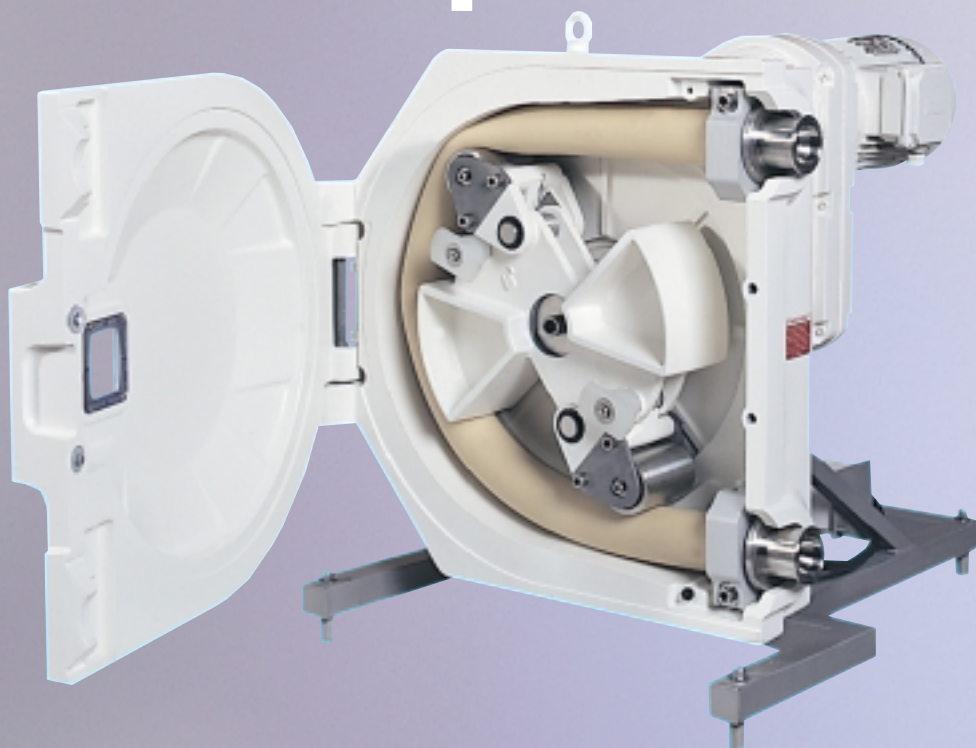
Specifications subject to change without notice. Printed and copyrighted by Sartorius Stedim Biotech GmbH
W/sart-000 - G
Publication No.: SPK2030-e08066
Order No.: 85030-511-67

WATSON
MARLOW
PUMPS

S E R I E S

800

High-flow **Hygienic** Pumps





Put Watson-Marlow to work on your pumping problems

■ Watson-Marlow peristaltic pumps are problem solving pumps, best applied where other pump types fail or frustrate. Watson-Marlow works only through trained engineers, and, wherever you are, they will work with you, using the experience of meeting and solving literally thousands of pumping problems.

■ As the largest peristaltic pump manufacturer, with a range of pumps and tubing for flow rates from microlitres per hour to thousands of litres per hour, we stand every chance of helping you, but if we cannot we will tell you.

■ If we can help, we will do whatever is necessary to prove to you that it will do the job. Any product we recommend, we will stand by completely, and if it fails to meet the agreed need, then that will be our problem and not yours.

Watson-Marlow leads the world in solving fluid handling problems with peristaltic pumping technology. The company is accredited for design and manufacture to ISO9001, and provides its customers with nothing less than the best products, service and knowledge. Watson-Marlow conducts its business ethically, and stands by its word, its recommendations and its products.



The benefits of peristaltic pumping

Compared to lobe pumps, diaphragm pumps, gear pumps and piston pumps, and every other type of pump, these are the advantages of Watson-Marlow pumps:

- 1 No contamination of the fluid.
- 2 No contamination of the pump.
- 3 Ideal for shear-sensitive and aggressive fluids.
- 4 Self-priming, dry-running.
- 5 No valves, seals or glands.
- 6 Automatic check valve action prevents backflow.

PERISTALTIC PUMPS ARE IDEAL FOR

- Abrasive and aggressive fluids
- Beverage dispensing
- Cell culture
- Fermentation
- Filtration and separation
- Food processing
- Industrial chemicals
- Inks and pigments
- Pharmaceuticals
- Photographic solutions
- Water treatment



Purchasers in the EU please note

825 and 840 pumpheads are specially designed for connection by the user to gearboxes of the users choice and they do not carry the **CE** mark. These pumpheads are supplied with "Declarations of Incorporation" as required by the EU Machinery Directive.

The B/RA and the RA bare shaft pumps carry the **CE** mark, but the complete motorised pump assembly must also carry the assembler's **CE** mark in addition to the Watson-Marlow **CE** mark.

Customers in EU member States must note that self assembly of machines carries with it the responsibility to ensure that the final working assembly complies with all the relevant EU safety directives and the assembler's **CE** mark is affixed on completion.

Common conversions

To go from	Multiply by	To get to
bar	14.50377	psi
inches	25.4	mm
deg C	$(1.8 \times C) + 32$	deg F
gal (IMP)	4.5460	litres
gal (US)	3.7854	litres
gal (IMP)	1.20095	gal (US)
gpm (US)	0.22712	m ³ /hr
gpm (IMP)	0.27276	m ³ /hr
inches Hg	1.1329	ft H ₂ O
inches Hg	0.4912	psi
kg/cm ²	14.22334	psi
kW	1.341	hp
kPa	0.14504	psi
N/m ²	1.0	Pa
Pa	0.00001	bar
litre	0.0001	m ³
kgcm	0.098	Nm

Standards

CE Conforms to all relevant Directives

IEC 335-1 is the International Electrotechnical Commission standard dealing with the "Safety of household and similar appliances, general requirements". Equivalents are BS3456: Part 101 and DIN VDE 0700: Part 1).

EN60529 is the European Norm standard dealing with the "Classification of degrees of protection provided by enclosures for rotating machines. Equivalents are BS 4999: Part 105, IEN 60034: Part 5, and DIN VDE 0530: Part 5. IP numbers (such as IP34, IP42, IP55) indicate the degree of ingress protection of the product, with the first digit indicating protection against the ingress of objects, and the second digit indicating the degree of protection against the ingress of water.

EN60204-1 is the European Norm covering "The Safety of Machines - Electrical Equipment of Machines".

EN61010-1 is the European Norm covering "Safety requirements for electrical equipment for measurement, control and laboratory use".

EN50081-1 is the European Norm covering "Electromagnetic compatibility - Generic Emission standard - Residential, commercial and light industry".

EN50082 - 1 is the European Norm covering "Electromagnetic compatibility - Generic Immunity standard - Residential, commercial and light industry".

Spare parts availability

Watson-Marlow's policy is to provide spare parts for all products for a minimum of eight years from discontinuation. For major products, this period is extended to twelve years. The ability to implement this policy is not entirely within Watson-Marlow's control and cannot be guaranteed, but every effort will be made to honour this policy.

825

25mm High-flow, hygienic pump

825

Provides 2000 litre/hr
(0.33 litre/rev)

Twin stainless steel rollers

Hinged door with only two
captive bolts makes
changing tube extremely
simple and safe

Use USP Class VI Bioprene
tubing for 2 bar (29 psi) and
3.5 bar (51 psi) operation

Tube elements complete
with hygienic connectors

Tubing in extended element
lengths for fitting customers
own connectors

Bareshaft pumpheads to
take a range of foot-
mounted motors with
flexible couplings

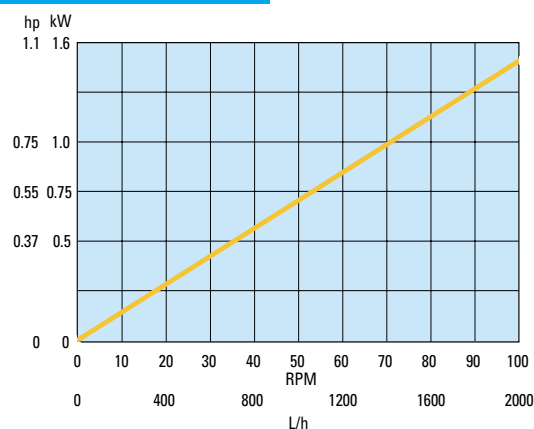
Pumpheads to accept IEC B5
output flange-mounted gear
motors



Standards

BS800, IEC 335-1,
EN60529 (IP55) CE

825R or B/R Motor power/tube life



Ordering information

Pumps

825B/R	Baseplate mounted bareshaft pumphead	080.2500.000
825RA	Pumphead with bareshaft adaptor (no baseplate)	083.2510.000

Bioprene tubing for 825 pumps

Tube bore				
25mm	1"	2 bar TM tube element	770mm length	088.0250.E0M
25mm	1"	3.5 bar TH tube element	770mm length	088.0250.E0H
25mm	1"	2 bar TM tube element	2.3m length	088.0250.00M
25mm	1"	3.5 bar TH tube element	2.3m length	088.0250.00H

Connectors for 825 pumps

825CT	Triclap hygienic connector	1"	089.0250.00T
825CS	SMS hygienic connector		089.0250.00S
825CI	IDF/ISS hygienic connector		089.0250.00R
825CQ	Quick coupling (MIL-C-2748F)	1"	089.0250.00Q
825CR	Quick RJT (BS1864) connector		089.0250.00R

Tube lubricant

400g	Translucent food machinery grease (USDA-H1) approved	098.0005.000
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Drive options

A number of motor/gearbox options and control options are available for these pumps including fixed and variable speed with mechanical variations. The options include inverter control enabling 4-20mA and 0-10V process control, remote stop/start and reverse, and frequency output.

Configurations

All 800 series pumps are available from Watson-Marlow as complete, ready to run, motorised pumps with a two year warranty.

Each pump supplied by Watson-Marlow is a fully assembled, ready-to-run unit, or a B/RA or an RA bare shaft, ready-to-drive pumphead, which complies with all relevant EU (European Union) safety directives and carries the relevant  mark or declaration of incorporation.

Fixed speed pumps

825 and 840 pumps can be supplied as a complete speed units fitted with an IP55 motor and gearbox in 4 different speeds.

825FB/R pump speeds are 22, 38, 68 and 98 rpm. 840FB/R pump speeds are 22, 39, 62 and 100 rpm.

Variable speed inverter controlled pumps

We supply complete electronically variable speed pumps with two maximum speeds with a 5:1 reduction ratio. The minimum flow rate will be approximately 20% of the maximum achievable.

Watson-Marlow have selected as standard accessories, single phase input/three phase output inverters for use with the 800 series pumps (maximum power requirement 1.5KW, for use with the 825 pumps and 2.2KW for use with 840 pumps).

All Watson-Marlow pumps are available fitted with motorised geared units to suit the users own choice of inverter.

Mechanically variable speed pumps

All Zone 1 Exd 800 series pumps and those rated above 2.2KW are fitted with belt driven mechanically variable speed gearboxes and IP55 standard motors.

Explosion-proof pumps

All pumps are available fitted with Exd IIB T4 specification explosion-proof motors that meet all EU explosion-proof standards. Specially selected combinations of explosion-proof motors and electronic inverters are available. These inverters are not fitted with explosion-proof casework and therefore must be sited outside the hazardous area.

Accessories

Pulsation dampers will be required for certain applications. Watson-Marlow will supply pulsation dampers from the Flowguard range.

Tube failure detectors are available to order.

A choice of feet or castors for fitting to 825 and 840 pump frames are available.

840

40mm High-flow, hygienic pump

840

Provides 8000 litre/h
(1.33 litre/rev)

Twin stainless steel rollers

Hinged door with two
captive bolts makes
changing tube extremely
simple and safe

Use USP Class VI Bioprene
tubing for 2 bar (29 psi) and
3.5 bar (51 psi) operation

Tube elements complete
with hygienic connectors or

Tubing in extended element
lengths for fitting customers
own connectors

Bareshaft pumpheads to
take a range of foot-
mounted motors with
flexible couplings

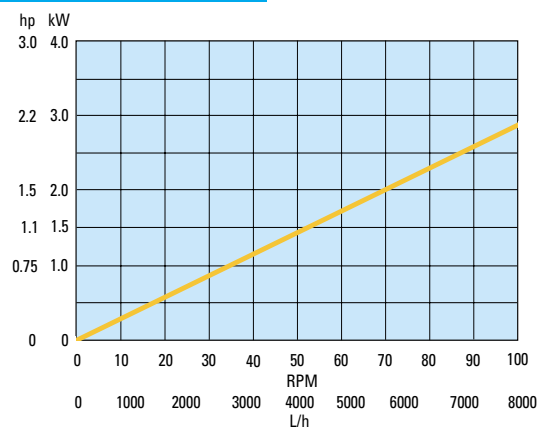
Pumpheads to accept IEC B5
output flange-mounted gear
motors



Standards

BS800, IEC 335-1,
EN60529 (IP55) CE

840R or B/R Motor power/tube life



Ordering information

Pumps

840B/RA	Baseplate mounted bareshaft pumphead	080.4000.000
840RA	Pumphead with bareshaft adaptor (no baseplate)	083.4010.000

Bioprene tubing for 840 pumps

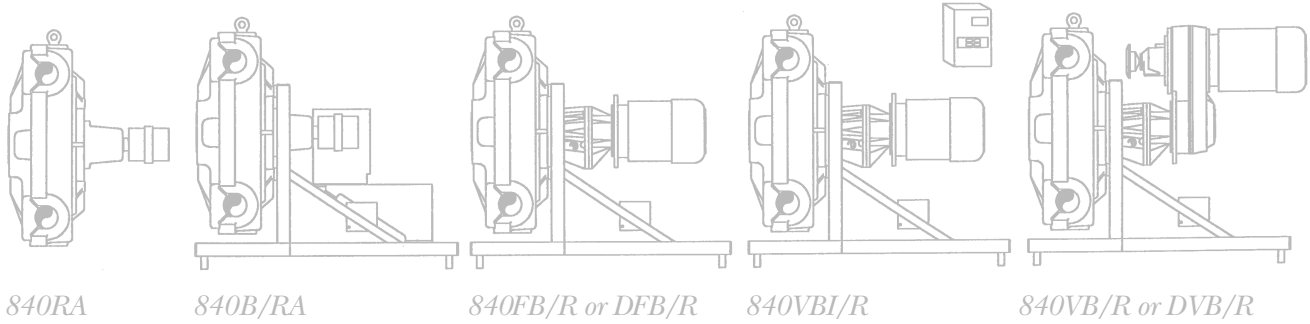
Tube bore			
40mm	1 1/8"	2 bar TM tube element	1.25m length
40mm	1 1/8"	3.5 bar TH tube element	1.25m length
40mm	1 1/8"	2 bar TM tube element	2.5m length
40mm	1 1/8"	3.5 bar TH tube element	2.5m length

Connectors for 840 pumps

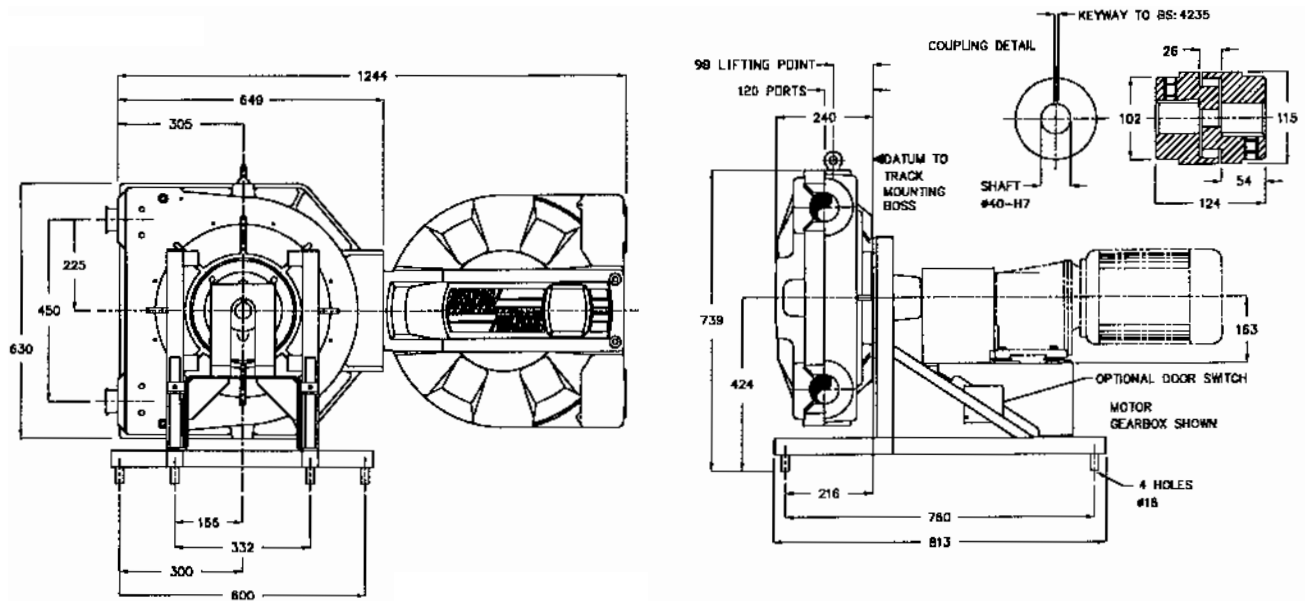
840CT	Triclamp hygienic connector	2"	089.0400.00T
840CS	SMS hygienic connector		089.0400.00S
840CI	IDF/ISS hygienic connector	2"	089.0400.00R
840CQ	Quick coupling (MIL-C-2748F)		089.0400.00Q
840CR	Quick RJT (BS1864) connector		089.0400.00R

Tube lubricant

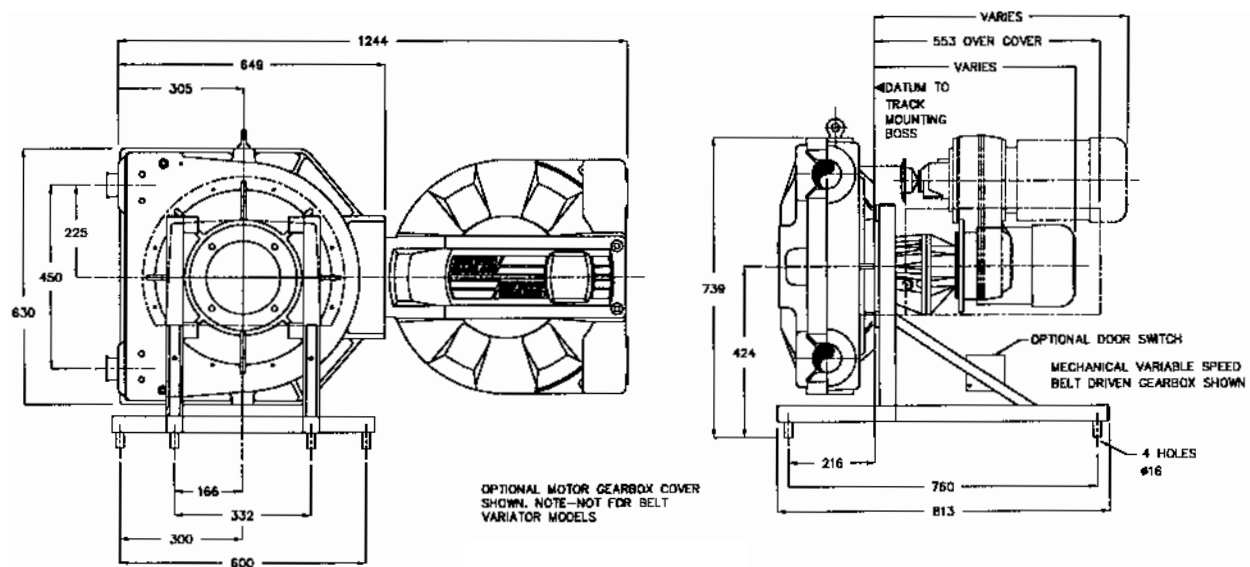
400g	Translucent food machinery grease (USDA-H1) approved	098.0005.000
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Dimensions mm



840B/RA



840FB/R, 840VBI/R, 840DFB/R, 840DVB/R

800

Connectors

800 series pumps may be used with either tube elements fitted with hygienic connectors or extended element lengths. A choice of connector types is offered, including Triclamp (Triclover and 3A compatible), IDF and SMS sanitary, and RJT. These are constructed from 316 stainless steel and are totally autoclavable.

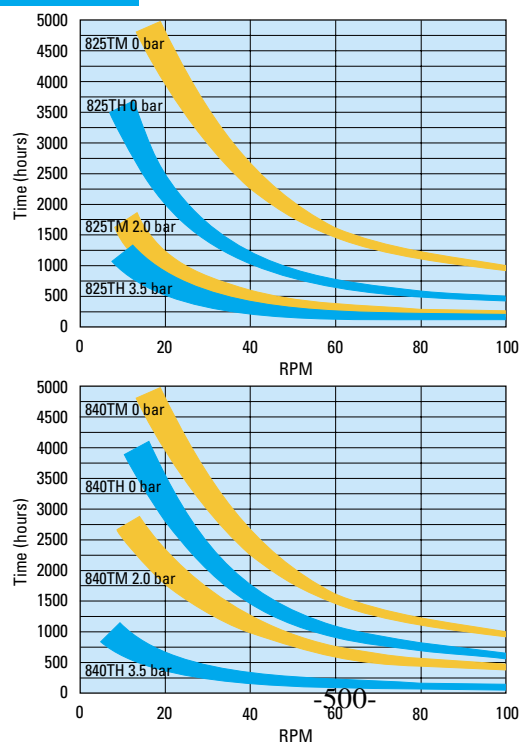
Operating and storage temperatures

Unless otherwise stated, all pumps listed in this brochure may be operated at ambient temperatures between 5°C and 40°C (41°F and 104°F). They may be stored at temperatures between -40°C and 70°C (-40°F and 158°F), but allow time for acclimatisation before operating.

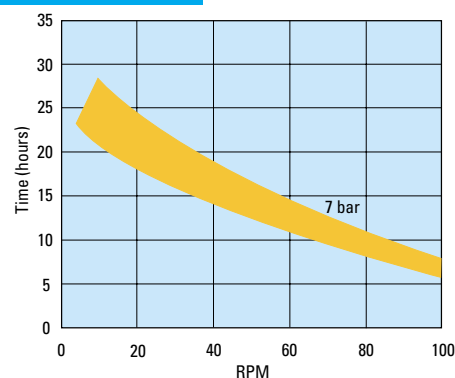
Flow rates

All flow rates quoted in this brochure were obtained pumping water at 20°C (68°F) with zero suction and delivery heads.

Tube life



High pressure tube life



Tubing

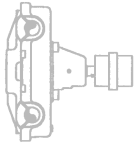
The Watson-Marlow 800 series pumps use a Bioprene tube which meets USP and NFS Class VI requirements. Bioprene also complies with FDA 21 CFR 177.260 and meets USDA standards for food handling.

High pressure applications

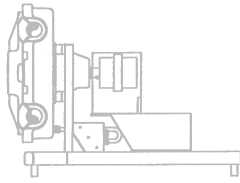
For specific higher pressure applications, use 3.5 bar "TH" tubing elements for intermittent periods only. Do not use quick connectors for this process. Tubing previously used as a pumping element should not be used as a transfer section.

Tube lubricant

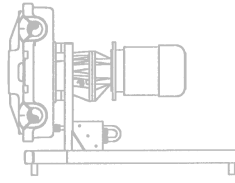
Translucent food machinery grease (USDA-H1 approved for food contact) is available for 800 series tubing to prolong tube life.



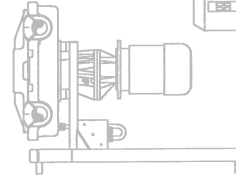
825RA



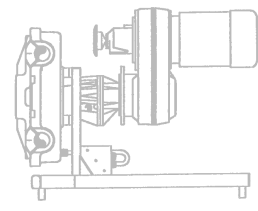
825B/RA



825FB/R or DFB/R

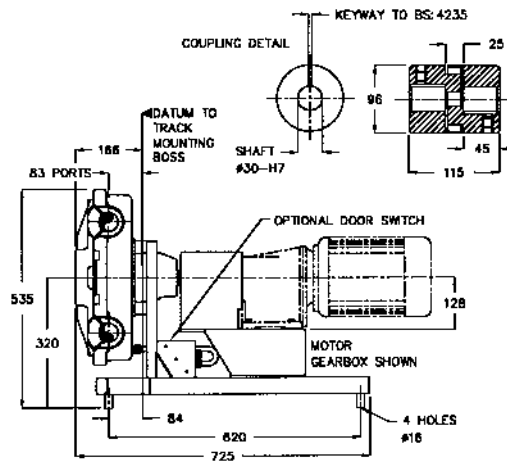
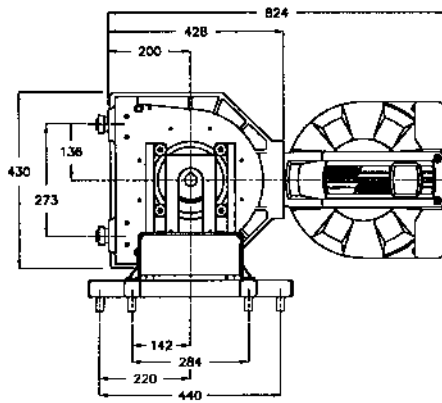


825VBI/R

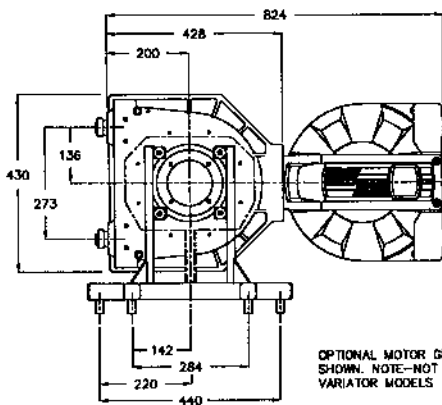


825VB/R or DVB/R

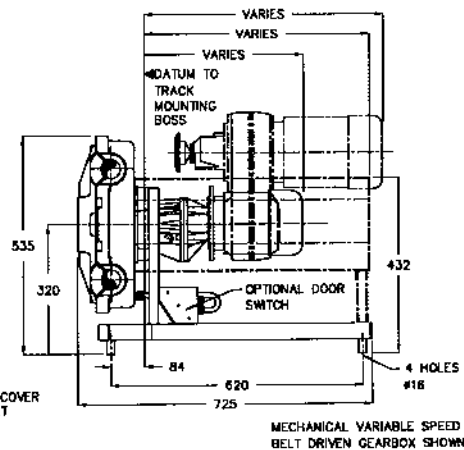
Dimensions mm



825B/RA



OPTIONAL MOTOR GEARBOX COVER SHOWN. NOTE--NOT FOR BELT VARIATOR MODELS



825FB/R, 825VBI/R, 825DFB/R, 825DVB/R

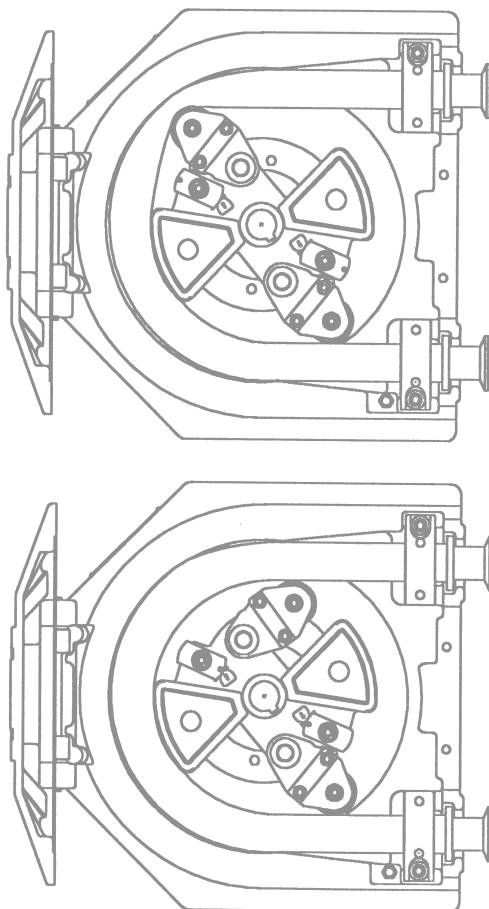
800

Materials of construction

Description	Material
Pumphead body	Aluminium alloy with epoxy polyester powder coat finish
Pumphead door	Aluminium alloy with epoxy polyester powder coat finish
Pumphead rotor	Aluminium alloy
Rotor rollers	316 stainless steel
Frame	Stainless steel 304L
Optional motor housing	Stainless-steel 304L
Door fixings	Stainless steel
Motor fixings	Zinc plated high tensile steel bolts, stainless steel nuts and washers
Frame fixings	Stainless steel

Paint specification

The 800 series epoxy polyester powder coating is based on a mixed polymer thermosetting resin designed to combine the durability associated with epoxies with the enhanced UV and heat stability associated with polyesters. This results in a high quality finish which is abrasive and impact resistant.



Installation drawings

Installation drawings of all 800 series pumps are available on request in A3 size. Reproducible drawings are also available for a modest fee.

Custom-built pumps

Watson-Marlow Limited's team of technical support engineers is available to advise and quote for your custom-built pumps with electric, hydraulic or pneumatic motors, trolley mounting, stainless steel baseplates etc.

CIP

The 800 series pumphead incorporates retractable roller mechanisms which allow clean-in-place or steam-in-place hose cleaning. The roller mechanisms are simply unlocked and disengaged from the standard pumping position, providing maximum cleaning capacity via a free flow of cleaning agents through the hose.

SIP

The 800 series can be steamed-in-place at 135°C (2 bar) for a duration of one hour. Allow 15 minutes for pump to return to ambient temperature prior to restarting pump.

Flow rates

Up to 8,000 litres/hour depending upon motor speed.

Pressures

Up to 3.5 bar continuous operation governed by motor sizing.

Drive options

Fixed speed, variable speed (inverter or mechanical variator), all drives available with Exd options. Contact Watson-Marlow Technical Support for further information.

Duty rating

24 hour governed by motor sizing.

825

25mm hygienic pumps



840

40mm hygienic pumps



The 800 series pumps have been designed for hygienic pumping up to 8000 litre/hour and pressures to 3.5 bar (51 psi), in the biotechnology, pharmaceutical and food industries. Pumpheads are constructed of aluminium with an epoxy powder coated white finish and they offer true CIP (clean-in-place) and SIP (steam-in-place) as the rollers retract to a non-occluding position, allowing a complete flow-through for cleaning.

All pumps are mounted on a stainless steel frame with the option of a brushed stainless steel motor housing, where belt variators are not required.

Watson-Marlow's focus has been to minimise the total cost of ownership over the lifetime of the pumps by making them reliable, long-lasting, and simple to use and maintain. Downtime is the true enemy of productivity, and so minimising downtime and whatever essential maintenance is required rewards our care and your choice of pump.

For instance and (uniquely), access to the tube is through a hinged door rather than a lift-off cover, and the door is secured by two captive bolts rather than sixteen or twenty loose ones, making tube changing fast, simple and safe.

Bioprene tube elements with hygienic connectors are autoclavable and can be fitted quickly and cleanly.

Where hygiene and system up-time is valued, there is no better pump than a Watson-Marlow 800 series.

**WATSON
MARLOW**

Unmatched warranties

The high quality of the design and manufacture of Watson-Marlow products allows us to offer international warranties far exceeding those available for other pump types.

All 800 series pumps carry a two year warranty.



WATSON MARLOW PUMPS

The information contained in this document is believed to be correct but Watson-Marlow Limited accepts no liability for any errors it contains, and reserves the right to alter specifications without notice.

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S E R I E S

100/200

Low-flow pumps

100 series flow rates from 0.01 to 53 ml/min. Single channel. Fixed and variable flow rates.



Multi-channel pumps

200 series flow rates from microlitres to 32 ml/min. through up to 32 channels. Manual and auto-control.



300

Low-cost pumps

Flow rates from 0.2 to 2,000 ml/min. Fixed and variable speeds.

● HB 0060



500

Microprocessor controlled pumps

Flow rates from 0.01 to 2,200 ml/min. 1 to 48 channels. Manual, auto and digital control.



IP55 rated pumps

Washdown pumps for tough environments, and pneumatic or baseplate-mounted pumps with Exd motors for hazardous areas. Flow rates to 2.2litre/min.

● HB 0062

600

Mid flow pumps

Cased pumps or baseplate-mounted pumps for flows up to 15.8 litre/min (4.2 US gpm). Fixed or variable speed and single channel.

● HB 0063



700

High-flow pumps

IP55 rated pumps with manual or auto control and baseplate-mounted industrial pumps provide flows to 2,000 litre/hr (8.8 US gpm). Single or twin channel.

● HB 0060



800

High-flow hygienic pumps

Use Bioprene USP Class VI tubing for flow rates up to 8,000 litre/hr (35 US gpm), and pressures up to 3.5 bar (50 psi). True CIP and SIP facilities ideal for biotech, pharmaceutical and food industries. Single channel.

● HB 0057



900

High-flow, high-pressure pumps

Use reinforced tubing in five different materials for flow rates up to 10,000 litre/hr and pressures up to 15 bar (210 psi). Single channel.

● HB 0056



Dispensers & Robotic fillers

For repetitive and accurate dosing and dispensing duties. Straightforward stop/start volumes up to one litre in five seconds or precision, balance-controlled dispensing.

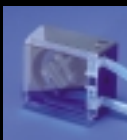
● HB 0039



OEM pumps

Pumpheads for use with customers' own drives or plate-mounted pumpheads and motors. Compact, easy to install and to use. Single and multi-channel with flow rates up to 2,700 ml/min.

● HB 0076



Tubing

Twelve different materials and over 50 sizes of tubing for the complete range of Watson-Marlow pumps. Full chemical compatibility tables with 450 fluids tabulated. Performance and physical data.

● HB 0065



Members of the Spirax-Sarco Engineering Group

Watson-Marlow is a registered trademark of Watson-Marlow Limited.

Publication ref: HB 0057

● These brochures describe the full Watson-Marlow range of peristaltic pumps, tubing and accessories.

ST DESIGN

BIOPRENE TUBING

Thermoplastic elastomer tubing

Highly resistant to oxidising agents

Validated processes

Bioprene peristaltic pump tubing is fully approved for food and pharmaceutical applications. Validated processes are supported. Like Marprene, Bioprene lasts at least 10 times as long as tubing in other materials. Long-life tubing means stoppages for a tube change are rare events, easily fitted in with general maintenance.

Easy sterilisation

Clean-in-place and steam-in-place (with tubing elements) are no problem for the tube that has everything.

USP, ISO and FDA approvals matter in maintaining validated processes. Bioprene peristaltic pump tubing offers long life and chemical resistance, and carries the widest range of safety approvals

- USP Class VI FDA approvals
- Fully documented bio-compatibility and comprehensive validation pack
- Safe for use in biomedical applications
- Ex-stock availability
- Comprehensive stock of a wide range of sizes
- UV opaque
- Fully weldable
- No odour
- Low extractables
- Suitable for repeated autoclave cycles

Watson-Marlow Bioprene: the best peristaltic pump tube life with excellent chemical resistance

For long life and chemical compatibility

Bioprene offers exceptionally long life and resistance to a wide range of chemicals. It is a first choice for applications including metering tablet-coating materials, pH control and media feed in fermentation and bioreactor metering, as well as pharmaceutical handling, dispensing, metering, transfer and filtration.

General industrial long-life transfer tube. Highly resistant to oxidising agents such as ozone, peroxides and sodium hypochlorite.

Bioprene	Typical values
Material	Thermoplastic elastomer
Colour / transparency	Beige / opaque
Spallation	Fair
Life, hours	313/314, 520R pumpheads: 10,000; 620R pumphead: 6,000
Certification	FDA regulations 21 CFR 177.2600 for contact with aqueous food
Sterilisation methods	Gamma, autoclave, EtO. CIP, SIP: refer to Watson-Marlow for details
Operating temperature	5C-80C
Hardness, shore A (5 sec)	64 shore: 66; 73 shore: 74; 87 shore: 88
Specific gravity	64 shore: 0.97; 73 shore: 0.96; 87 shore: 0.95
Tear B, ppi	-
Ultimate tensile strength, psi	64 shore: 1007; 73 shore: 1410; 87 shore: 2263
Elongation at break, %	64 shore: 473; 73 shore: 510; 87 shore: 547
Tensile stress at 100% elongation, psi	64 shore: 367; 73 shore: 525; 87 shore: 987
Compression set, %	-
Weather resistance	Excellent
Sunlight resistance	Excellent
Gas permeability, O ₂ cc.cm x 10 ⁻⁴ / cm ² .sec.atm	5.8
Gas permeability rating	Fair
Water absorption	Good
Odour	Excellent
ASTM methods	Hardness: ASTM D 2240; Specific gravity: ASTM D 792; Tear B, Ultimate tensile strength, Elongation at break, Tensile stress at 100% elongation: ASTM D 412

Bore		Wall		Coil size	Part number	Coil size	Part number	Coil size	Part number
inch	mm	inch	mm						
1/50	0.5	1/16	1.6	50ft / 15m	903.0005.016	16ft / 5m	903.0005.J16	500ft / 152m	903.0005.R16
1/32	0.8	1/16	1.6		903.0008.016		903.0008.J16		903.0008.R16
1/16	1.6	1/16	1.6		903.0016.016		903.0016.J16		903.0016.R16
3/32	2.4	1/16	1.6		903.0024.016		903.0024.J16		903.0024.R16
1/8	3.2	1/16	1.6		903.0032.016		903.0032.J16		903.0032.R16
3/16	4.8	1/16	1.6		903.0048.016		903.0048.J16		903.0048.R16
1/4	6.4	1/16	1.6		903.0064.016		903.0064.J16		903.0064.R16
5/16	8.0	1/16	1.6		903.0080.016		903.0080.J16		903.0080.R16
					903.0005.024		903.0005.J24		
					903.0008.024		903.0008.J24		
1/16	1.6	3/32	2.4	50ft / 15m	903.0016.024	10ft / 3m	903.0016.J24	Custom sizes are available to order, as are other specific requirements	903.0016.R24
1/8	3.2	3/32	2.4		903.0032.024		903.0032.J24		903.0032.R24
3/16	4.8	3/32	2.4		903.0048.024		903.0048.J24		400ft / 122m 903.0048.R24
1/4	6.4	3/32	2.4		903.0064.024		903.0064.J24		300ft / 91m 903.0064.R24
5/16	8.0	3/32	2.4		903.0080.024		903.0080.J24		200ft / 61m 903.0080.R24
3/8	9.6	3/32	2.4		903.0096.024		903.0096.J24		150ft / 46m 903.0096.R24
					903.0048.032		903.0048.I32		
1/4	6.4	1/8	3.2		903.0064.032		903.0064.I32		200ft / 61m 903.0064.R32
3/8	9.6	1/8	3.2		903.0096.032		903.0096.I32		150ft / 46m 903.0096.R32
1/2	12.7	1/8	3.2		903.0127.032		903.0127.I32		
5/8	15.9	1/8	3.2	903.0159.032	903.0159.I32				
-	8.0	-	4.0	903.0080.040	903.0080.I40				
-	12.0	-	4.0	903.0120.040	903.0120.I40				
-	16.0	-	4.0	903.0160.040	903.0160.I40				
3/8	9.6	3/16	4.8	903.0096.048	903.0096.I48				
1/2	12.7	3/16	4.8	903.0127.048	903.0127.I48				
5/8	15.9	3/16	4.8	903.0159.048	903.0159.I48				
3/4	19.0	3/16	4.8	903.0190.048	903.0190.I48				
1	25.4	3/8	4.8	903.0254.048	903.0254.I48				

Bioprene for validation

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Members of the Spirax-Sarco Engineering Group

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WARNING These products are not designed for use in, and should not be used for, patient-connected applications.

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Value for life



PRODUCTS

ABEC Integrated Solutions

Bioreactors/Fermenters

Media/Buffer Process Modules

Separation/Purification

Single Use Systems

Stainless Technology

Mission

Products and Services

Bioreactors/ Fermenters

Since our inception, ABEC has been the industry leader in the design, engineering and manufacture of high quality custom Bioreactors and Fermenters. During this time, we are proud of the many innovations in mechanical design and process improvements that have been widely adopted by the industry world wide and are now common elements in bioreactor design.

Some of these innovations include:

- The standard use of electropolishing to ensure continuous and cleanable surfaces for all process lines.
- The inherently aseptic non-pressurized seal housing design utilizing a tandem (in-line) double mechanical seal which is lubricated by non-pressurized clean steam condensate.
- The use of bottom mounted, offset agitation to eliminate the necessity of using baffles to ensure proper mixing and easy-to-achieve sterility following the CIP/SIP steps.
- The low shear "elephant ear" impeller, combined with the offset agitation, ensures gentle, top to bottom mixing for uniform cell growth.



Jacketed Tanks

Our cylindrical jacketed tanks are custom made to satisfy your process, mixing, and temperature control requirements. Built from 304, 304L, 316, or 316L stainless steel. Our jacketed tanks can be easily adapted to meet your dimensional requirements. All standard sizes have optional features that allow for made-to-order applications.

Features at a glance:

- Standard sizes 18 to 7,000 gallon
- 304, 304L, 316, 316L stainless steel
- 2B, #4/180, #7/320, and electropolish available
- Flat, sloped, dished, or 15 ° cone bottom
- ASME or non-ASME code stamped designs
- Jackets available: embossed, dimple, half pipe, laser
- Jacket design: pressure 150 psi, temperature 366° F



Sharpsville Container is known for high quality fabrication in stainless steel and exotic alloys. Our vessels, whether they are process or transport, ASME, UN, or Heat Transfer are manufactured for the Food, Chemical, Beverage, Petro-Chemical and Pharmaceutical markets. The size of vessels that we manufacture range from 1 gallon to 25,000 gallons. With our standard line and custom design expertise, we are capable of meeting or exceeding your fabrication requirements. Our reputation for quality and service continues to exceed our customers' expectations.



ISO 9001 Certified

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www.sharpsvillecontainer.com



STANDARD TANK OPTIONS: CHECK ALL THAT APPLY

OUTLET OPTIONS

SHROUD: YES ☐ NO ☐
 REGULATION: YES ☐ NO ☐
 INSULATION/SHROUD THICKNESS ("F"): 1-1/2" ☐ 2" ☐

TOP HEAD: NONE ☐ LOOSE COVER (SEE SHT 2) ☐ DOME ☐ FLAT ☐ CONE ☐

SHROUD/REGULATION "E": 1" ☐ 1/2" ☐ 3/4" ☐ 1" ☐ 1 1/2" ☐ 2" ☐ 3" ☐ 4" ☐ 6" ☐ 8" ☐ 10" ☐ 12" ☐ 14" ☐ 16" ☐ 18" ☐ 20" ☐ 22" ☐ 24" ☐ 26" ☐ 28" ☐ 30" ☐ 32" ☐ 34" ☐ 36" ☐ 38" ☐ 40" ☐ 42" ☐ 44" ☐ 46" ☐ 48" ☐ 50" ☐ 52" ☐ 54" ☐ 56" ☐ 58" ☐ 60" ☐ 62" ☐ 64" ☐ 66" ☐ 68" ☐ 70" ☐ 72" ☐ 74" ☐ 76" ☐ 78" ☐ 80" ☐ 82" ☐ 84" ☐ 86" ☐ 88" ☐ 90" ☐ 92" ☐ 94" ☐ 96" ☐ 98" ☐ 100" ☐ 102" ☐ 104" ☐ 106" ☐ 108" ☐ 110" ☐ 112" ☐ 114" ☐ 116" ☐ 118" ☐ 120" ☐ 122" ☐ 124" ☐ 126" ☐ 128" ☐ 130" ☐ 132" ☐ 134" ☐ 136" ☐ 138" ☐ 140" ☐ 142" ☐ 144" ☐ 146" ☐ 148" ☐ 150" ☐ 152" ☐ 154" ☐ 156" ☐ 158" ☐ 160" ☐ 162" ☐ 164" ☐ 166" ☐ 168" ☐ 170" ☐ 172" ☐ 174" ☐ 176" ☐ 178" ☐ 180" ☐ 182" ☐ 184" ☐ 186" ☐ 188" ☐ 190" ☐ 192" ☐ 194" ☐ 196" ☐ 198" ☐ 200" ☐ 202" ☐ 204" ☐ 206" ☐ 208" ☐ 210" ☐ 212" ☐ 214" ☐ 216" ☐ 218" ☐ 220" ☐ 222" ☐ 224" ☐ 226" ☐ 228" ☐ 230" ☐ 232" ☐ 234" ☐ 236" ☐ 238" ☐ 240" ☐ 242" ☐ 244" ☐ 246" ☐ 248" ☐ 250" ☐ 252" ☐ 254" ☐ 256" ☐ 258" ☐ 260" ☐ 262" ☐ 264" ☐ 266" ☐ 268" ☐ 270" ☐ 272" ☐ 274" ☐ 276" ☐ 278" ☐ 280" ☐ 282" ☐ 284" 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BTAX 215

Separation system for Pharmaceutical and Biotechnical applications

The BTAX centrifuge is specially designed for biotechnical processes such as cell harvesting, broth clarification and the separation of cell debris. The centrifuge has a very high separation efficiency and can be installed in a closed system. To ensure cleanliness, the BTAX can be heat pasteurised to 100°C.

Available models

The BTAX centrifuge is available in four versions

- BTAX 215S-31 CEP
Paring disc version.
- BTAX 215S-31 CEFP
Paring disc version, explosion protected.
- BTAX 215H-31 CEP
Hermetic version.
- BTAX 215H-31 CEFP
Hermetic version, explosion protected.

All BTAX models are gastight. The complete system can be supplied in an explosion-protected version when required.

Throughput capacity

Actual throughput is in the range of 0-12 m³/h depending on paring disc size and design, as well as on the amount and type of solids in the feed, temperature, viscosity, required degree of clarification etc. Max hydraulic capacity of disc stack is much higher.

Efficient solids ejection

During separation, solids collect in pockets recessed in the bowl wall which avoids undesirable solids build-up, and minimizes disturbances during solids ejection. The pneumatically operated solids-ejecting system ensures fast and efficient discharges resulting in a clean bowl.

Axial discharge channels lead from the solids pockets to valves, which are held closed by a spring loaded valve slide. To eject solids from the bowl during operation the slide is lowered momentarily by a very short injection of compressed air or gas through the hollow bowl spindle. This opens the valves and the solids are ejected.



High separation efficiency

The high speed of the bowl creates a peripheral centrifugal acceleration of 12,000 gravities. This gives the BTAX an extremely high separation efficiency that can capture particles down to 0.1 µ in diameter.

Large solids space

Long periods between ejections is possible thanks to the large (14 l) solids space, which results in better separation and drier solids.

Paring disc design

In this version the clarified liquid is continuously discharged under pressure by a paring disc, which is a stationary impeller that converts the rotational energy of the liquid into pressure. With the paring disc design there is no need for a down-stream pump.

Hermetic inlet and outlet

The bowl is always completely filled with liquid in the hermetic version. This eliminates the risk for oxidation and airborne infections and ensures gentle treatment of the product.

Efficient cooling

The frame hood and bowl casing are jacketed for cooling. When separated solids need to be cooled, a jacketed cyclone can be supplied.

Totally contained system

To protect both the product and environment, the BTAX 215 is provided with a special water cooled axial seal under the bowl to prevent contamination of the drive system.

Sturdy frame and belt drive

Power is transmitted from the vertically mounted motor to the spindle cartridge by the flat-belt drive inside the sturdy frame. The vertical bowl spindle which supports and drives the separator bowl is designed as a replaceable cartridge unit.

Material

All liquid-wetted parts are made of high-grade stainless steel. The bowl body and the valve slide are made of steel quality, specially developed to resist corrosion and with the high

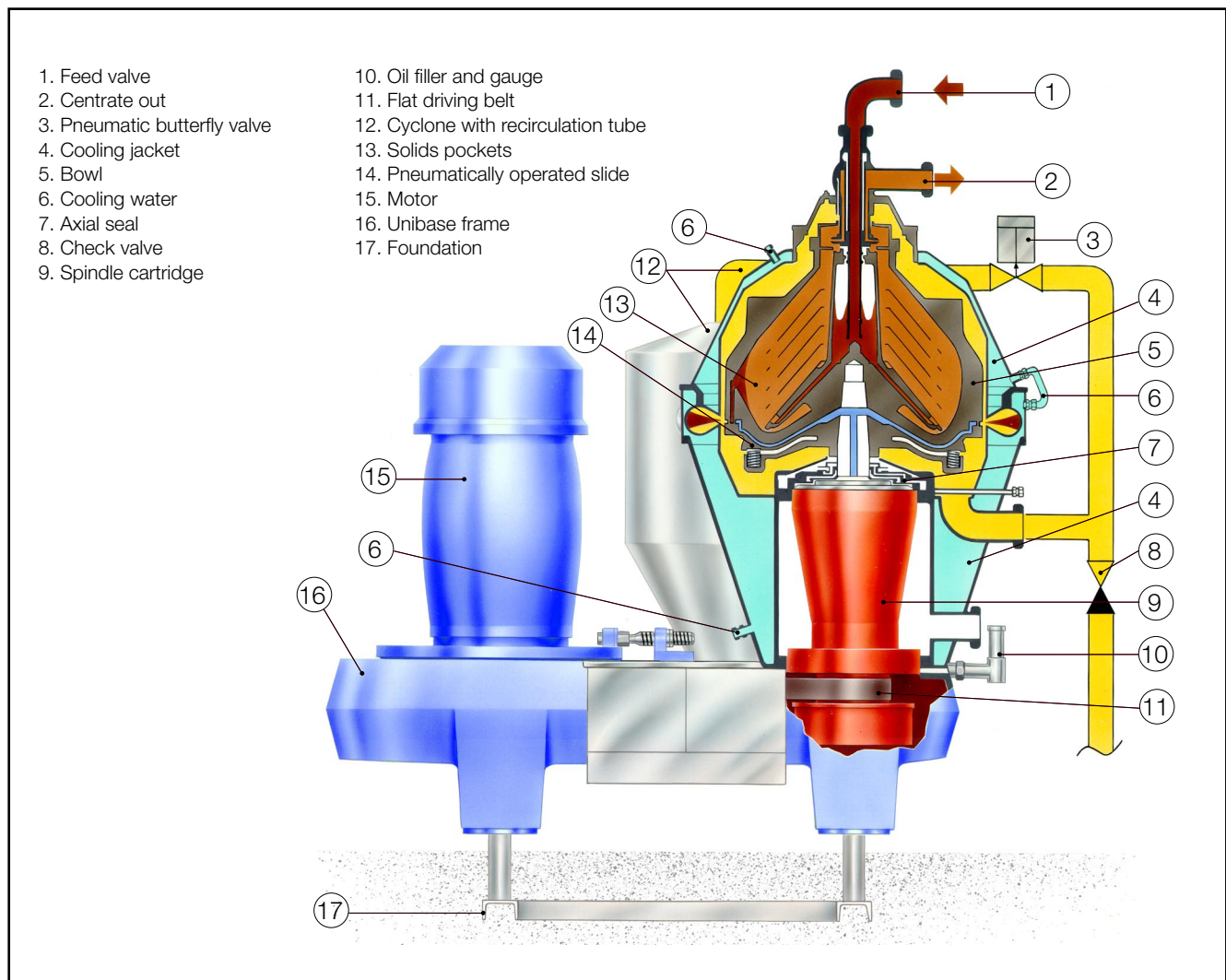
tensile strength needed for the high g-force generated in the BTAX centrifuge. The frame hood, solids receptacle and cyclone as well as bowl casing are of stainless steel and the frame is epoxy-enamelled cast iron. Gaskets are of EPDM, Viton or Nitrile.

Standard equipment

Centrifuge with electric motor, small or large cyclone. The large cyclone has cooling jacket, sight glass and connections for level transmitter. Foundation frame and vibration dampers, tank for compressed air with solenoid valve for discharge, vibration monitor and speed transmitter, oil pressure gauge and switches, one set of tools and one intermediate service kit.

Optional equipment

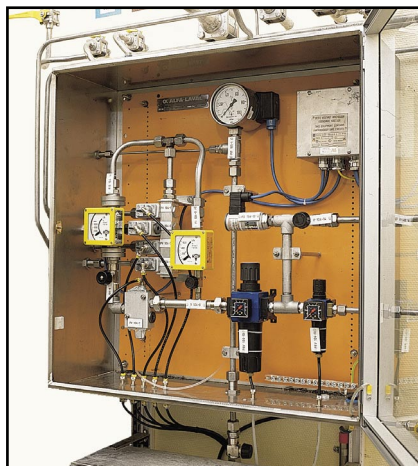
Cover interlock switch, special tools for cartridge, intermediate and major service kit, cartridge service kit and service kit for foundation feet.



Cross-section of BTAX 215 paring disc version



Control and starting equipment (not explosion-protected).



Inert gas regulating unit.



Valve module and service liquid unit.

Ancillary equipment necessary for operation

Electrical and pneumatic system consisting of

- Starting equipment with y/d-starter, DC-brake and main switch.
- Control equipment:
 - A. Not explosion protected version with built-in operator's control panel. A remote control panel is available as an option, or
 - B. explosion protected version including a simple control cabinet to be placed outside the hazardous area and an operator's control panel to be placed in the hazardous area.
 - C. Pneumatic unit with solenoid valves, pressure reducing valves and pressure switch. Normal and explosion-protected versions are available.

Valve module including inlet valves for either safety liquid or process feed, and outlet valves to direct the centrifugate to either drain or process outlet. Also included is a flow transmitter and regulating valve for the feed and a counter pressure regulating valve for the outlet.

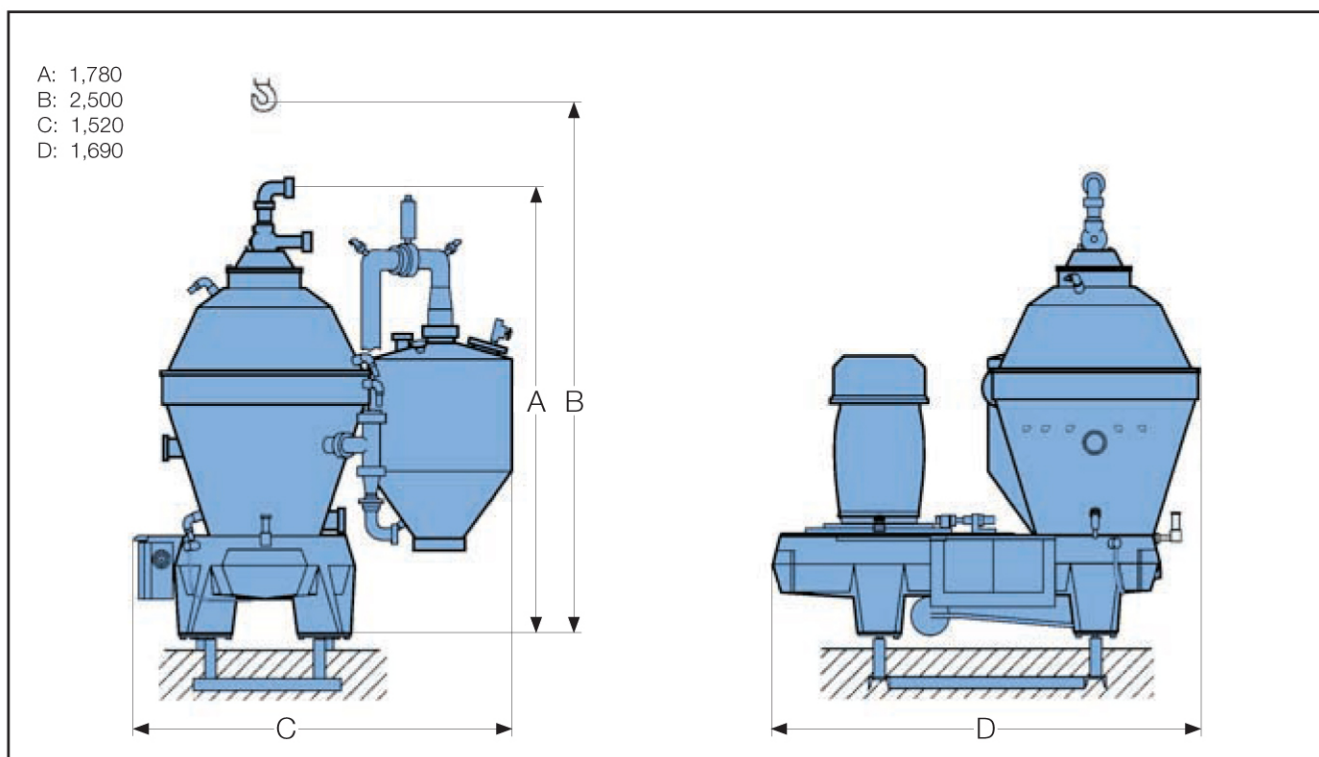
Service liquid unit with valves to control flushing, cooling and sealing liquid. Flow switches for the sealing liquid are also included.

For centrifuges explosion protected with inert gas the following additional units are needed:

- A. Inert gas regulating unit with valves and flow-switches for flow control.
- B. Seal pot unit to give slight overpressure in the whole system.
- C. Solids receiving unit with pneumatic pump to handle the discharged solids.

Technical data

Motor size	
Standard	30 kW, controlled torque
Explosion protected	30 kW, controlled torque
EEx de IIB T4	
Throughput and power consumption	
Paring disc version	
Small paring disc	0-5 m ³ /h, 10-17 kW
Large paring disc	2-12 m ³ /h, 15-25 kW
Hermetic version	0-12 m ³ /h, 13-28 kW
Starting time	approx 7 minutes
Stopping time	
With DC brake	approx 20 minutes
Max bowl speed	6,065 rpm
Solids space volume	14 litres
Caulk thickness	0.4 mm
Cooling water consumption	
Cooling jacket	200-400 l/h
Hermetic seal	60-80 l/h
Axial seal	30 l/h
Cyclone with cooling jacket	200-400 l/h
Gas consumption for solids discharge	20 NI/discharge
Max. pasteurization temperature	100°C
Discharge valve	24 VDC, 24 VAC, 48 VAC, 110 VAC, EEx d IIC T5
Inert gas consumption	
For purging	20 Nm ³ /h
For normal operation	100-400 NI/h



Dimensions. Measurements in mm.

Shipping data

Centrifuge with motor and set of tools

Net weight	2,100 kg
Gross weight	2,450 kg
Volume	8 m ³

LS00017EN 0409

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How to contact Alfa Laval

Contact details for all countries are continually updated on our website. Please visit www.alfalaval.com to access the information direct.

Sartocube® – Hydrosart® Ultrafilter Cassette

Protein purification, concentration and diafiltration



Description

The Hydrosart® Membrane

Hydrosart is a stabilized cellulose based membrane that has been optimized for the biotechnological and pharmaceutical industry. The Hydrosart membrane is a stable polymer that features a broad pH range. Hydrosart is also extremely hydrophilic, making it non-protein binding, virtually non-foul, and has extremely high flux. Membrane regeneration, storage and depyrogenation can be accomplished by using NaOH even at elevated temperatures. These features make Hydrosart an ideal membrane for biological applications. Hydrosart ultrafiltration Sartocube® cassettes are available in the following nominal molecular weight cutoffs: 10 kD | 30 kD

Applications

Hydrosart ultrafiltration membranes are designed for use in the biotechnological and pharmaceutical industries. They can be used for the following applications:

- Oligonucleotide
- Proteins
Albumin, even with 40% EtOH
Hemoglobin
- Coagulation factors
Factor VIII
Factor III
- Vaccines
Tetanus
Diphtheria
- Monoklonal Antibodies

Product profile

Hydrosart shows minimal adsorption of proteins, viruses, etc. Membrane retention is unaffected by repeated re-use.

The Hydrosart ultrafiltration membrane can be re-used without any less cleaning loss of integrity or performance.

Feature	Benefits
Non-adsorptive	No loss of proteins, easy to clean, sustained flux
Non-protein binding	High product yield
Wide pH and temperature range	More choices in sanitizing agents
High flow rates	Economical filtration runs
Self sealing cassette	No gaskets needed
Silicone sealing compound	No glue
Enlarged inlet and outlet holes	Lower pressure drop

Better solvent resistance than Polyethersulfone and Cellulose Triacetate

Specifications

Materials of construction

Membrane	Hydrosart (stabilized cellulose based membrane)
Gaskets	PVDF
Spacer	Polypropylene
Sealing compound	Silicone

Pore size | Retention rate

Hydrosart ultrafiltration cassettes are available in a choice of the following nominal molecular weight cut offs: 10 kD | 30 kD

Available sizes

Sartorius Crossflow Cassettes are available in **Standard Cassette** size for pilot- | production scale and in **Sartocon Slice** format for reduced volume handling.

Available filterholder

Sartorius Crossflow Cassettes are designed for Sartorius filter holders like, Sartocon, Sartocon 2 Plus, Sartocon 3, and different Sartoflow holder.

Filtration area

Filter area Sartocube® Cassette is 3.0 m²

Operating parameters

Feed pressure, P _{in}	58 psi 4 bar maximum
Operating temperature	50 °C maximum, at 20 °C
Max. air diffusion rates at P _{in} = 15 psi 1 bar	50 ml air/min for 3.0 m ² filter area
Cleaning	NaOH, 1 M, 40 °C
Disinfection	NaOH, 1 M, 40 °C, 30 min
Storage	NaOH, 0.1 M

Sartorius Crossflow Filter

Sterilization

NaOH, 1 M, 40 °C, 30 min

Regulatory compliance

All materials have passed the current USP Biological Test. The filtrate meets or exceeds USP and EP requirements for Sterile Water for Injection with respect to total solids, oxidizable substances, particulate matter, ammonia, chloride, nitrate, sulfate and heavy metals.

Quality control

Each filter cassette is individually assigned a serial number, integrity tested and certified.

It complies with cGMP requirements for non-fiber-releasing filters and is filed under the Drug Master File Number DMF 5967 by the Food and Drug Administration, Washington, DC. Validation information is available upon request.

If you use holding devices from other suppliers, please contact our Applications Department. A different torque might be needed due to specific variations in design.

For further assistance, please contact your local Sartorius field engineer or our Goettingen- based Applications Department in Germany.

Technical references:

Validation Guide

Publication No.: SPC5704-e

Directions for Use (Sartocube® Cassettes)

Publication No.: SPC6018-a

Typical water flux release data*

Nominal molecular weight cutoff (kD) Sartocube® Cassettes 3.0 m² filter area Permeate* [l/h]

10 kD 190

30 kD 600

* (Feed pressure, P_{in} = 22 psi | 1.5 bar; Retentate pressure, P_{out} = closed valve; P_{Filtrate} = open valve)

Retention rates Hydrosart®

Substance	Approx. Mol. Wt.	2 kD	5 kD	10 kD	30 kD	100 kD
Vitamin B12	1.200	≥88%	–	–	–	
Inulin	5.000	–	>97%	–	–	
Cytochrome C	12.400	–	–	>97,5%	–	
Albumin	67.000	–	–	–	>97,5%	≤60%
γ Globulin	169.000	–	–	–	>97,5%	≥96%

Order information

Available types and order numbers

Type	Filter area	Cut off	Order no.
Sartocon Cassettes	3.0 m ²	10 kD	302 144 39 30 E-BSW
Sartocon Cassettes	3.0 m ²	30 kD	302 144 59 30 E-BSW

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Order No.: 85030-523-55



Hydrosart® Ultrafiltration Cassettes

Protein purification, concentration and diafiltration



Description

The Hydrosart® Membrane

Hydrosart is a stabilized cellulose based membrane that has been optimized for the biotechnological and pharmaceutical industry. The Hydrosart membrane is a stable polymer that features a broad pH range. Hydrosart is also extremely hydrophilic, making it non-protein binding, virtually non-foul, and has extremely high flux. Membrane regeneration, storage and depyrogenation can be accomplished by using NaOH even at elevated temperatures. These features make Hydrosart an ideal membrane for biological applications. Hydrosart ultrafiltration cassettes are available in the following nominal molecular weight cutoffs: 2 k | 5 k | 10 k | 30 k

Applications

Hydrosart ultrafiltration membranes are designed for use in the biotechnological and pharmaceutical industries. They can be used for the following applications:

- Oligonucleotide
- Proteins
Albumin, even with 40% EtOH
Hemoglobin
- Coagulation factors
Factor VIII
Factor III
- Vaccines
Tetanus
Diphtheria
- Monoclonal Antibodies

Product profile

Hydrosart shows minimal adsorption of proteins, viruses, etc. Membrane retention is unaffected by repeated re-use.

The Hydrosart ultrafiltration membrane can be re-used without any less cleaning loss of integrity or performance.

Feature	Benefits
Non-adsorptive	No loss of proteins, easy to clean, sustained flux
Non-protein binding	High product yield
Wide pH and temperature range	More choices in sanitizing agents
High flow rates	Economical filtration runs
Self sealing cassette	No gaskets needed
Silicone sealing compound	No glue
Enlarged inlet and outlet holes	Lower pressure drop
Better solvent resistance than Polyethersulfone and Cellulose Triacetate	

Specifications

Materials of construction

Membrane	Hydrosart (stabilized cellulose based membrane)
Gaskets	PVDF
Spacer	Polypropylene
Sealing compound	Silicone

Pore size | Retention rate

Hydrosart ultrafiltration cassettes are available in a choice of the following nominal molecular weight cut offs: 5 k | 10 k | 30 k

Available sizes

Sartorius Crossflow Cassettes are available in **Standard Cassette** size for pilot- | production scale and in **Sartocon Slice** format for reduced volume handling.

Available filterholder

Sartorius Crossflow Cassettes are designed for Sartorius filter holders like SartoconSlice (0.1 m² Cassettes only), Sartocon, Sartocon 2 Plus, Sartocon 3, and different Sartoflow holder.

Filtration area

Filter area Sartocon Cassette	0.6 m ²
Filter area Sartocon Slice Cassette	0.1 m ²

Operating parameters

Feed pressure, P _{in}	58 psi 4 bar maximum
Operating temperature	50 °C maximum, at 20 °C
Max. air diffusion rates at P _{in} = 15 psi 1 bar	15 ml air/min for 0.6 m ² filter area 5 ml air/min for 0.1 m ² filter area
Cleaning	NaOH, 1 M, 40 °C
Disinfection	NaOH, 1 M, 40 °C, 30 min
Storage	NaOH, 0.1 M

Sartorius Crossflow Filter

Sterilization

NaOH, 1 M, 40 °C, 30 min

Regulatory compliance

All materials have passed the current USP Biological Test. The filtrate meets or exceeds USP and EP requirements for Sterile Water for Injection with respect to total solids, oxidizable substances, particulate matter, ammonia, chloride, nitrate, sulfate and heavy metals.

Quality control

Each filter cassette is individually assigned a serial number, integrity tested and certified.

It complies with cGMP requirements for non-fiber-releasing filters and is filed under the Drug Master File Number DMF 5967 by the Food and Drug Administration, Washington, DC. Validation information is available upon request.

If you use holding devices from other suppliers, please contact our Applications Department. A different torque might be needed due to specific variations in design.

For further assistance, please contact your local Sartorius field engineer or our Goettingen- based Applications Department in Germany.

Technical references:

Validation Guide
Publication No.: SPC5701-e

Directions for Use (Sartocon Cassettes and Sartocon Slice Cassettes)
Publication No.: SPC6001-a

Typical water flux release data*

Nominal molecular weight cutoff (k)	Sartocon Cassettes 0.6 m ² filter area Permeate* [l/h]	Sartocon Slice Cassettes 0.1 m ² filter area Permeate* [l/h]
2 k	7	1.5
5 k	12	3
10 k	35	8
30 k	120	25

* (Feed pressure, P_{in} = 22 psi | 1.5 bar; Retentate pressure, P_{out} = closed valve; P_{Filtrate} = open valve)

Retention rates Hydrosart®

Substance	Approx. Mol. Wt.	2 k	5 k	10 k	30 k
Vitamin B12	1.200	≥88%	–	–	–
Inulin	5.000	–	>97%	–	–
Cytochrome C	12.400	–	–	>97,5%	–
Albumin	67.000	–	–	–	>97,5%

Order information

Available types and order numbers

Type	Filter area	Cut off	Order no.
Sartocon Cassettes	0.6 m ²	2 k	302 144 19 06 E--SG
Sartocon Cassettes	0.6 m ²	5 k	302 144 29 06 E--SG
Sartocon Cassettes	0.6 m ²	10 k	302 144 39 06 E--SG
Sartocon Cassettes	0.6 m ²	30 k	302 144 59 06 E--SG
Sartocon Slice Cassettes	0.1 m ²	2 k	305 144 19 01 E--SG
Sartocon Slice Cassettes	0.1 m ²	5 k	305 144 29 01 E--SG
Sartocon Slice Cassettes	0.1 m ²	10 k	305 144 39 01 E--SG
Sartocon Slice Cassettes	0.1 m ²	30 k	305 144 59 01 E--SG

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Order No.: 85030-509-91



Sartocon® 2Plus Stainless Steel Holder

Crossflow holder for Sartocon® cassettes



Description

Sartocon 2Plus Holder

The Sartocon 2Plus stainless steel holder is optimized for the use with up to ten Sartocon production scale Crossflow cassettes (max. 7 m²). It is designed for applications from 30 l to 1000 l volume.

Target use:

- process development
- preclinical trials
- clinical trials
- pilot lots

Sartocon cassettes with a filter area of up to 0.7 m² each, are available with Polyethersulfone, Hydrosart, Polypropylene and Cellulose Triacetate membrane types.

The Sartocon 2Plus system covers the whole range of pharmaceutical and biotechnological crossflow applications like concentration and diafiltration of proteins, vaccines, viruses, antibodies, oligo nucleotides, endotoxin removal etc. The system is also suitable for cell harvesting and clarification processes. The family of Sartorius Crossflow holders feature the latest advances in crossflow design:

- vertical orientation of cassettes
- self draining systems
- autoclavable and inline steamable
- no welds
- minimized hold up volume

The Sartocon 2Plus holding device is part of a modular micro- and ultrafiltration system and fits up to ten Sartocon filter cassettes. It is designed for process development and pilot scale production in pharmaceutical and biotechnology applications. Easy handling design and high quality materials make this holder the perfect tool.

The Sartocon cassettes are placed between filter and clamping plate without a need for additional gaskets. It's not even necessary to remove the clamping plate for installation of the cassettes. Just place the cassettes on the guide rods and close the holder with a torque wrench.

The vertical positioning of the cassettes allows complete draining of retentate and permeate channels by gravity during harvesting and steaming procedures.

Thermal sterilisation in an autoclave or steaming in place even with cassettes installed is possible. A special pressure compensation tool was designed to allow thermal sterilisation of Sartocon filter cassettes in the Sartocon 2Plus device.

The Sartocon 2Plus's flow distribution plate is machined from a single piece of stainless steel. It's sanitary 1 1/2" tri-clamp connections are not welded but machined from the same plate. This eliminates potentially problems associated with welds and ensures long service life and safe and reliable connection to other equipment.

The feed and retentate connectors are located on one side of the plate. This allows easy integration into any skid design and assures a compact system with low minimum working volume.

Connectors are situated to eliminate potential air locks and to assure thorough cleaning and total product recovery.

The Sartocon 2Plus device is available in a grinded and an electro polished surface version.

Feature	Benefits
Cassettes in vertical position	self draining
Tri-clamp connectors	safe fit of accessories
No welds	no corrosion
Steamable	no cross contamination
Fits up to ten Sartocon cassettes	high flexibility for up to 1000 l working volume

Specifications

Materials of Construction

Filter and Clamping plate	316L (1.4404) Stainless steel
Connectors	1"-1 1/2" sanitary Tri Clamp flange (DN25)
Nuts for tie rods	Nickel coated bronze
Other components	316L Stainless steel

Sartorius Crossflow Holder

Technical Data

Surface finish	Ra ≤ 0.6 µm
Maximum number of cassettes	10 Sartocan cassettes
Dimensions (L × W × H)	371 × 270 × 348 mm
Weight	approx. 50 kg

Ordering Informations and Accessories

Sartocan 2Plus stainless steel holder, grinded	17546---002
Sartocan 2Plus microfiltration set	17546---201
Sartocan 2Plus ultrafiltration set	17546---202
Sartocan 2Plus stainless steel holder, electro polished	17546E--002
Torque wrench for Sartocan 2Plus holder	17128
Socket, 27 mm	6986135
Pressure gauge, 0-6 bar, 1-1 1/2" autoclavable	17546---003
Diaphragm valve, 1-1 1/2"	17546---005
Silicone gasket (FDA), 1-1 1/2"	17546---012
Clamp for 1-1 1/2" Tri Clamp	17033
Sartocan 2Plus manifold for permeate outlet	17546---016
Hose connector to 1-1 1/2" Tri Clamp flange	17546---018
Pressure compensation tool for steaming and autoclaving	17625

Ultrasart Cassettes

Membrane Material	Nominal Molecular Weight Cutoff [NMWCO]	Order Numbers Sartocan®
Cellulose triacetate	5 kD 20 kD	3021452907E--SG 3021454907E--SG
Polyethersulfone (PESU)	1 kD 5 kD 8 kD 10 kD Albumin Albumin (New) 30 kD 50 kD 100 kD 300 kD	3021460907E--SG 3021462907E--SG 3021463407E--SG 3021463907E--SG 302146AL07K--SG 302146AL07K--SW 3021465907E--SG 3021465007E--SG 3021466807E--SG 3021467907E--SG
Hydrosart®	2 kD 5 kD 10 kD 30 kD 100 kD	3021441906E--SG 3021442906E--SG 3021443906E--SG 3021445906E--SG 3021446806E--SG

Microsart Cassettes

Membrane Material	Pore Size [µm]	Order Numbers Sartocan®
Polyethersulfone (PESU)	0.1 µm	3021545806W--SG
Polypropylene	0.2 µm	3021750706W--SG
Hydrosart®	0.2 µm 0.45 µm	3021860706W--SG 3021860606W--SG
Hydrosart® Open Channel	0.2 µm 0.45 µm	30218607040--SG 30218606040--SG

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Order No.: 85030-530-84

Sartocon 2 Plus Benchtop Crossflow System



Description

The Sartocon 2 Plus Benchtop is a basic cost effective Crossflow filtration system for small to intermediate scale Micro and Ultrafiltration pharmaceutical and biotech applications.

The Sartocon 2 Plus Benchtop is mainly used in Process Development laboratories and Pilot plants to run small production and clinical lots. The system is designed for membrane areas of 0.4 to 2.5 m² but can accommodate upto 10 Sartorius Sartocon Cassettes.

The Sartocon 2 Plus Benchtop is supplied complete with a tank, CIP sprayball, sanitary diaphragm valves, temperature and pressure gauges. The design and engineering of the system is equivalent to a large scale production system.

Sartocon filter cassettes utilize a parallel leaf design which provides the user with linear scale-up and predictable performance for future production needs. Therefore, the flow characteristics of a 5 square foot system are the same as the flow characteristics of a 500 square foot system.

Sartorius offers standard systems like the Sartocon Benchtop as well as custom designs for laboratory, pilot plant and manufacturing.

Sartocon Benchtop System Advantages

- Compact foot print means you can locate the system almost anywhere
- Low operating volumes let you concentrate to < 1L
- Sanitary design makes this system ideal for cGMP production
- Low point drain facilitates recovery all of your product
- Integrity test port provides quick confirmation of the system's "ready status"
- Every unit is designed for easy cleaning in place

Documentation provided:

The system is supplied complete with a cGMP turn over package.

Specifications

Pump Output	>50 L/min @ 60 psi
Filter Area	4 to 70 ft ²
Tank Volume	20L
Min. Operating Volume	<1L
Max. Inlet Pressure	60 psi
Piping Connections	Tri-clamp
Electrical Req	115 VAC/15 Amps
Dimensions	2.5 feet X 3 feet

Components

316L SS Sartocon 2 Plus Holder
316L SS Feed Tank
316L SS Rotary Lobe Pump
316L SS Tubular Frame
316L SS Sanitary Pressure Gauges
316L SS Fractional Diaphragm Valves
316L SS Temperature Gauge

Sartorius Crossflow Filter

Quality and Documentation

Sartorius Crossflow filtration systems are manufactured from high quality components and designed to meet the strict requirements of cGMP operating environments.

All valves, tubing, instruments and filter holder wetted surfaces are 316 L SS electropolished with a surface finish < 20µ inch Ra.

All non wetted surfaces have a 150 grit electropolish finish and all welds are ground smooth to prevent corrosion.

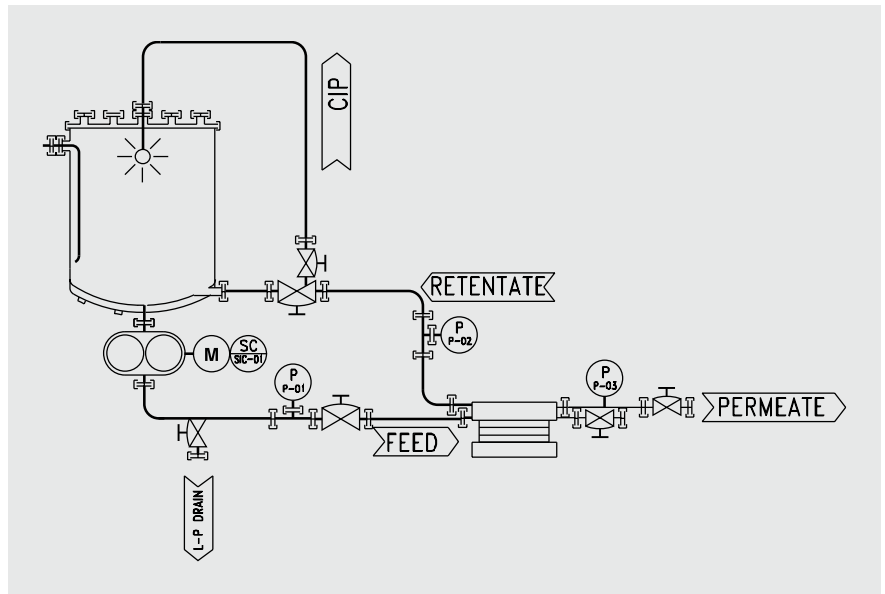
Standards and Codes

All fluid pathway components and manufacturing methods meet or exceed the current 3A Sanitary Standards "Accepted Practices for Permanently Installed Sanitary Products - Pipelines and Cleaning Systems".

All electrical enclosures are NEMA 4 and all electrical components are UL and CSA listed.

Ordering Information

Sartocon 2 Plus U1-SYS17546BT1-P3



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Publication No.: S--2037-am04051
Order No.: 85030-520-33



Life Sciences

MEMBRApplan® DG(M) – Safer Production and Higher Profitability



Filtration. Separation. Solution.

522

CLEAR SOLUTIONS - MEMBRApplan® DGM



The Best Solution for the Pharmaceutical and Biotechnological Production

Lead by innovation

Pall SeitzSchenk Filtersystems GmbH located in Bad Kreuznach and Waldstetten is a modern company for the filtration of chemical, pharmaceutical, and biotechnological products on an international scale. Due to its high performance level and worldwide presence Pall SeitzSchenk Filtersystems belongs to the leading companies in the field of filtration.

A row of basic inventions and fundamental product developments brought worldwide appreciation and contributes to the high standards of the Pall SeitzSchenk filtration technique.

Safety, efficiency, delivery readiness, service, technical consultancy, and high quality have always been the corner stones for Pall SeitzSchenk. The Pall SeitzSchenk filter systems are used around the world providing reliable and economical filtration.

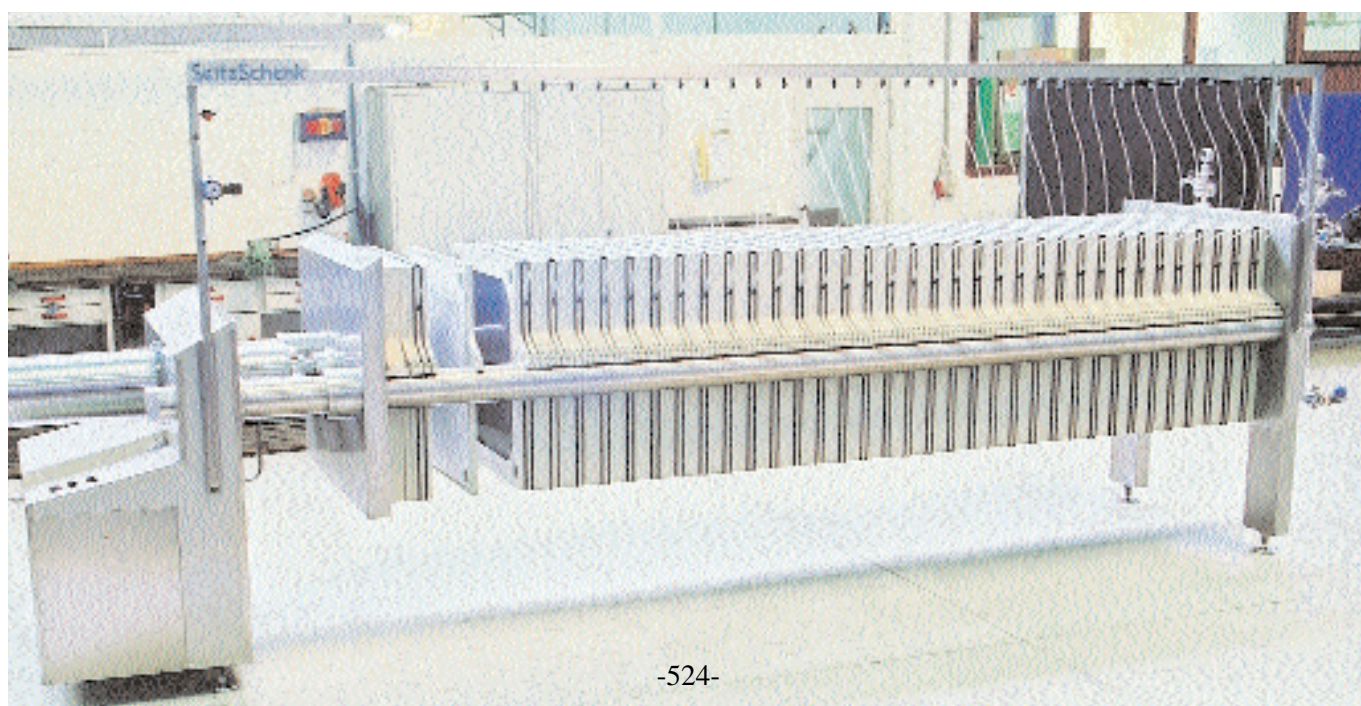
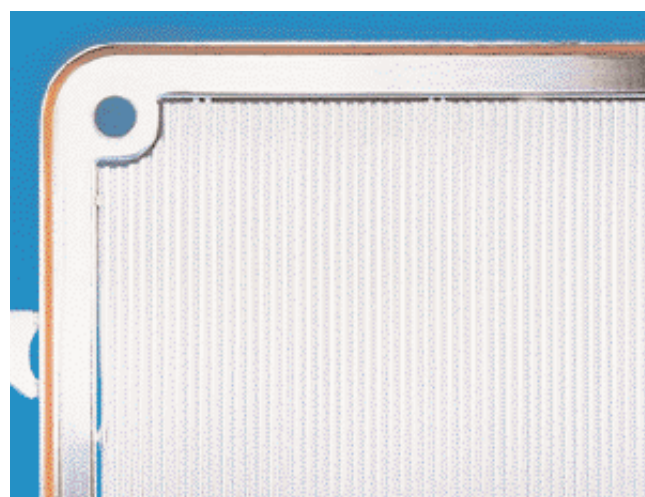
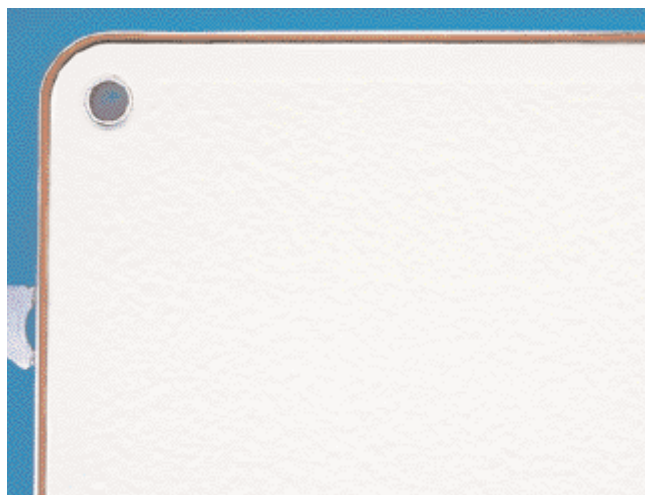
With the MEMBRAPlan® a completely new generation of sheet filters was developed, setting new standards for the modern pharmaceutical and biotechnological production. This new filtration method not only meets today's requirements, but also the requirements on future pharmaceutical processes.

The reason for the development of the MEMBRAplan® DG(M) was the need for a new type of filter for the treatment of parenteral pharmaceuticals with a high yield of the active ingredients. The result was a system which can be used for both a quantitative solid/liquid separation as well as for clarifying and final filtration.

The scope of potential applications is wide. For this reason only a few are mentioned:

- Plasma fractionation
- Biomass separation
- Removal of absorbents
- Removal of filter aids
- Removal of extraction residues
- Removal of catalysts
- Filtration of nutrients filtration of cell cultures
- Filtration of therapeutical proteins, vaccines, diagnostics, enzymes
- Filtration of antibiotics
- Adsorptive filtration

MEMBRAplan® DG(M) is the first system of its kind allowing a complete CIP cleaning and sterilization and thus meets all requirements of pharmaceutical equipment.





Technical Data MEMBRApplan DGM... P (with stainless steel filter plates)

Chassis size MEMBRApplan DGM	Depth filters	No. of		Membrane plates	Filter area m²	Filter cake volume * L
		15 mm frames	Filter plates			
400 P 30	8	8	4	4	1,0	11,2
	16	16	8	8	1,9	22,9
400 P 60	20	20	10	10	2,4	28
	30	30	15	15	3,6	42
400 P 100	40	40	20	20	4	60
	50	50	25	25	5	75
600 P 50	6	6	3	3	1,9	22,3
	18	18	9	9	5,6	67,0
	26	26	13	13	8,1	97,0
600 P 100	36	36	18	18	11,2	134
	50	50	25	25	15,5	186
600 P 150	58	58	29	29	18,0	216
	76	76	38	38	23,6	273
600 P 200	88	88	44	44	27,3	327
	100	100	50	50	25	372
800 P 50	6	6	3	3	3	36
	18	18	9	9	9	108
	26	26	13	13	13	156
800 P 100	36	36	18	18	18	216
	50	50	25	25	25	300
800 P 150	58	58	29	29	29	348
	76	76	38	38	38	456
800 P 200	88	88	44	44	44	528
	100	100	50	50	50	600

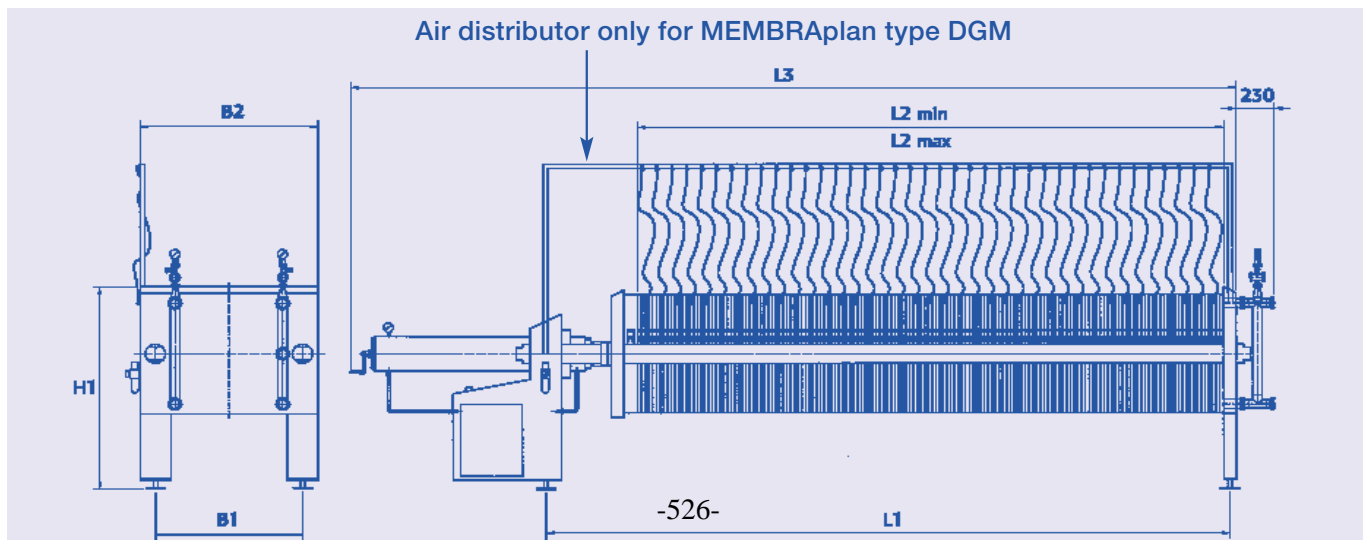
*) Only usable to 90%

Materials

Materials	
Chassis, parts in contact with product	Aisi 316 L
Filter pack	Polypropylene + Stainless steel
Membrane	Thermoplastic rubber
Gaskets (O-ring)	Silicone / EPDM / Viton™
™ Trademark Dupont	

Dimensions (in mm)

MEMBRApplan DG(M) with PP-plates	L ₁	L _{2min}	L _{2max}	L ₃	B ₁	B ₂	H ₁ *
MEMBRApplan DG(M) 400 K 30	1200	520	920	1920	470	550	1000
MEMBRApplan DG(M) 400 K 60	1950	1150	1650	2750	470	550	1000
MEMBRApplan DG(M) 400 K 100	2870	1970	2570	3760	470	550	1000
MEMBRApplan DG(M) 600 K 50	1900	940	1440	2660	720	940	1090
MEMBRApplan DG(M) 600 K 100	3100	1860	2660	4160	720	940	1090
MEMBRApplan DG(M) 600 K 150	4250	2810	3810	5510	720	940	1090
MEMBRApplan DG(M) 600 K 200	5450	4010	5010	6760	720	940	1090
MEMBRApplan DG(M) 800 K 50	2040	940	1440	2775	950	1150	1400
MEMBRApplan DG(M) 800 K 100	3270	1970	2670	4155	950	1150	1400
MEMBRApplan DG(M) 800 K 150	4420	2820	3820	5600	950	1150	1400
MEMBRApplan DG(M) 800 K 200	5620	4020	5020	6800	950	1150	1400
MEMBRApplan DG(M) with stainless steel-plates	L ₁	L _{2min}	L _{2max}	L ₃	B ₁	B ₂	H ₁ *
MEMBRApplan DG(M) 400 P 30	920	220	620	1610	470	550	1000
MEMBRApplan DG(M) 400 P 60	1420	620	1120	2210	470	550	1000
MEMBRApplan DG(M) 400 P 100	2020	1120	1720	2910	470	550	1000
MEMBRApplan DG(M) 600 P 50	1370	530	930	1990	720	940	1090
MEMBRApplan DG(M) 600 P 100	2160	1220	1720	2820	720	940	1090
MEMBRApplan DG(M) 600 P 150	2900	1670	2470	3970	720	940	1090
MEMBRApplan DG(M) 600 P 200	3660	2220	3220	4920	720	940	1090
MEMBRApplan DG(M) 800 P 50	1530	520	920	2270	950	1150	1400
MEMBRApplan DG(M) 800 P 100	2330	1120	1720	3580	950	1150	1400
MEMBRApplan DG(M) 800 P 150	3080	1670	2470	4430	950	1150	1400
MEMBRApplan DG(M) 800 P 200	3880	2270	3270	5430	950	1150	1400





	Filter pack	Plate thickness (mm)	Filter area per filter plate m²	Cake volume L	Weight (kg)
MEMBRAPlan DG(M) 400 P	Filter plate	10	0,24	-	3,8
	Membrane plate	14	-	-	-
	Frame	12	-	1,44	3,8
	Frame	25	-	3,0	7,9
	Frame	40	-	4,8	12,7
MEMBRAPlan DG(M) 400 K	Filter plate	25	0,2	-	3,5
	Membrane plate	34	-	-	5,5
	Frame	15	-	1,5	1,5
	Frame	20	-	2,0	2,0
	Frame	25	-	2,5	2,5
	Frame	40	-	4,0	4,0
MEMBRAPlan DG(M) 600 P	Filter plate	10	0,62	-	8,0
	Membrane plate	14	-	-	-
	Frame	12	-	3,72	6,5
	Frame	25	-	7,75	13,5
	Frame	40	-	12,40	21,7
MEMBRAPlan DG(M) 600 K	Filter plate	25	0,5	-	7,7
	Membrane plate	34	-	-	10,0
	Frame	15	-	3,75	2,0
	Frame	20	-	5,0	2,7
	Frame	25	-	6,25	3,4
	Frame	40	-	10,0	5,4
MEMBRAPlan DG(M) 800 P	Filter plate	10	1,0	-	12,0
	Membrane plate	14	-	-	-
	Rahmen	12	-	6,0	10,0
	Rahmen	25	-	12,5	20,8
	Rahmen	40	-	20,0	33,3
MEMBRAPlan DG(M) 800 K	Filter plate	25	0,84	-	12,5
	Membrane plate	34	-	-	15,5
	Rahmen	15	-	6,3	3,0
	Frame	20	-	8,4	4,0
	Frame	25	-	10,5	5,0
	Frame	40	-	16,8	8,0

EXAMPLE: MEMBRAPlan DGM		DG	M	C	800	K	100
Enclosed filter system with O-ring sealing arranged on the periphery of the plate	G = enclosed filter system with O-ring						
Membrane retightening	M = Membrane plate						
optional:	execution for the chemical industry						
Depth filter sizes:	300 = 30 x 30 cm (on request) 400 = 40 x 40 cm 600 = 60 x 60 cm 800 = 80 x 80 cm 1000 = 100 x 100 cm (on request)						
Filter plates:	K = Polypropylene P = Stainless steel						
Chassis size:	30, 50, 60, 100, 150, 250, 300, 400, 500, 600, 800, 1000 (for 600/800 depth filter format)						



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Reorder Code. PLS-P124 engl. 3 07/03



Chromaflow columns

Chromaflow™ columns are a family of convenient to use, process-scale columns. A patented nozzle in the top and bottom of the column allows packing, unpacking, and cleaning when fully assembled, that is with the lid in place. Chromaflow columns simplify chromatographic procedures and offer:

- convenience
- saving of labor
- reproducibility
- contained packing
- scalability

General column description

Chromaflow low-pressure columns (Fig 1) are available in a choice of dimensions and materials. The complete range offers inner diameters (i.d.) from 300 to 2000 mm (Table 1), with column tubes manufactured from cast acrylic (Fig 1). All dimensions are available with variable bed heights, providing a wide variety of bed volumes. All columns are pressure rated for operation at 3 bar.

Chromaflow columns incorporate a patented, pack-in-place nozzle (Fig 2) through which process liquids enter and exit. Manual or automated versions of the nozzles are available. The automated nozzle is controlled from the packing station or the nozzle control unit. The nozzle has three positions to facilitate the different aspects of column operation: packing, operation, unpacking and cleaning. In addition to this pack-in-place functionality, the nozzle also contains the process liquid flow path to provide a consolidated solution to the process stream handling.

Bed supports are available in 316L stainless steel or polyethylene. The multilayer, woven stainless steel bed supports have very high chemical resistance and longevity for use in applications where salt concentrations are low and pH is above 5. Polyethylene bed supports are recommended for applications with low pH and high salt concentrations. All other wetted parts in columns with polyethylene bed supports are manufactured from plastic or noncorrodible materials for use in low pH /high salt applications.



Fig 1. A Chromaflow column, 2000 mm i.d.



Fig 2. The Chromaflow nozzle that enables packing in place in a fully assembled column (GE Healthcare patent).



The construction materials include 316L stainless steel, acrylic, polypropylene, polyethylene, PEEK 450 G, EPDM rubber and FEP encapsulated silicone. These materials have high chemical resistance to the liquids typically used in process chromatography (Table 2). Furthermore, all polymeric materials are approved according to USP class VI tests for toxicity.

As an option, a dedicated packing station is available for Chromaflow columns. The packing station speeds up the packing procedure by eliminating the more time-consuming, manual maneuvers (Fig 3).

Comprehensive documentation is delivered with each column and includes a User manual, a Maintenance manual, assembly drawings, a full spare part list, materials certificates etc.

A Validation Support File containing information on column component composition, materials of construction and toxicity studies is also available.



Fig 3. Packing Chromaflow columns with the dedicated packing station is convenient and simple.

Convenient and labor saving

Once the column is assembled and the lid in place, no lifting gear is required for packing, operation, unpacking or cleaning-in-place (CIP). This means that a single operator can perform all column operations, thereby reducing labor costs and increasing convenience in large-scale operations.

Reproducibility

Packing with the lid in place allows the packing parameters to be easily set and fixed. Manual operation is minimized and standard operating procedures can be followed, helping to give reproducible column packing and results.

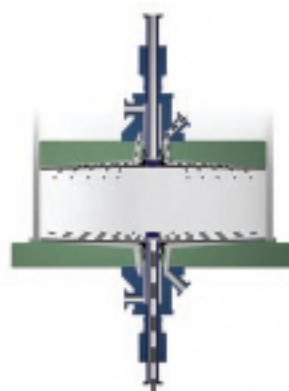
Contained packing

Improved safety is another advantage of the Chromaflow column concept. Because all the column operations are performed in a "closed system" environment, there is less risk of the operator coming into contact with hazardous chemicals and of the target product being exposed to contamination. In this way, overall safety and hygienic operation are improved.

Principle of operation

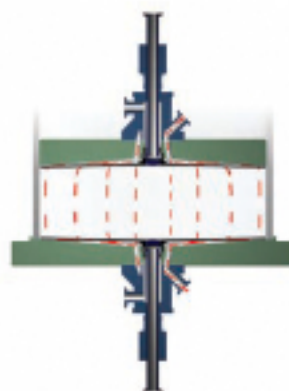
The column has a three-position nozzle located in the center of the top and bottom bed support. These three positions enable packing, unpacking, operation and cleaning to be performed without any adjustments to the assembled column, that is the lid remains in place.

Flow profiles from the two nozzles are identical. Packing direction will depend on the characteristics of the media and packing method used. The three positions are illustrated in Figure 4.



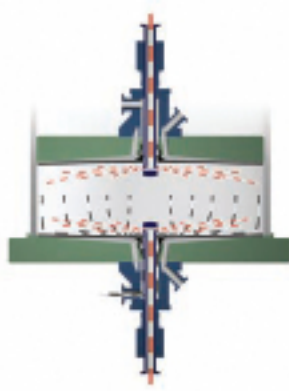
Packing position

The bottom nozzle is extended part of the way (mid position) into the column. The top nozzle is fully retracted. Slurry enters the column via the bottom nozzle and excess liquid exits via the top mobile phase outlet. After packing, the slurry lines are isolated from the mobile phase and can be cleaned independently from the rest of the column.



Running position

The bottom and top nozzles are retracted. Mobile phase enters the column directly into an annulus, immediately behind the bed support. The annulus is cut through at an angle to ensure that linear flow is kept constant during distribution of the mobile phase across the bed.



Unpacking position

In this position, both bottom and top nozzles are fully extended into the column thereby exposing a third passage through which medium leaves the column.

Cleaning solution can be pumped through the nozzles and sprayed into the column. In this way the column is easily and effectively cleaned without exposing the interior or the medium to the environment, and without dismantling the column.

Fig 4. The three positions of the Chromaflow nozzle showing packing from the top.

Scalability

Chromaflow columns are available in a wide range of dimensions, all designed and constructed around the same design principle. Standard range columns come in dimensions from 400 to 1000 mm, for more information about columns and dimensions, see Ordering information. Scaling up a chromatographic process from small to larger diameters is easily performed with maintained reproducibility, safety and convenience.

Column dimensions

A selection of Chromaflow columns in the range 400 to 2000 mm i.d. are presented in Table 1. The adapter stroke length is a standard 200 mm. Variable bed heights are available in the ranges 100–300 mm, 200–400 mm and 300–500 mm.

Chromaflow 400 SFP columns

Chromaflow 400 SFP (small flow path) columns are specially designed for low-flow applications. The dimensions in the mobile phase have been optimized to reduce dead volumes to a minimum and the area behind the nozzle tip has also been reduced.

Column materials and their chemical resistance

Table 2 lists the major components of Chromaflow columns in contact with process fluids (wetted parts) and Table 3 lists the chemical resistance of materials using data compiled from several published sources. It is important to note that columns with stainless steel bed supports and other stainless steel wetted components must be appropriately maintained when exposed to NaCl. Since salt can be corrosive to stainless steel over time, it is recommended that residual salt is removed by rinsing columns with at least five column volumes (CV) of clean water.

Table 1. Weights, volumes and dimensions for variable bed height Chromaflow columns

Description	Max operating pressure (bar)	Volume (l)	Column overall height (mm)	Weight, dry (kg)	Footprint (mm x mm)
Chromaflow column 400/100-300*	3	12.6–37.8	1568	230	700 x 700
Chromaflow column 600/100-300	3	28.3–84.9	1568	375	800 x 800
Chromaflow column 800/100-300	3	50.3–150.9	1572	610	1000 x 1000
Chromaflow column 1000/100-300	3	78.5–235.5	1573	930	1200 x 1200
Chromaflow column 1200/100-300	3	113.1–339.3			
Chromaflow column 1400/100-300	3	153.9–461.7			
Chromaflow column 1600/100-300	3	201.1–603.3			
Chromaflow column 1800/100-300	3	254.5–763.5			
Chromaflow column 2000/100-300	3	314.2–942.6			

* The first figure in the column name indicates the inner diameter and the second figure indicates stroke length.

Table 2. Major components and their composition

Component	Material	In contact with process stream
Column tube	Acrylic or stainless steel 316L	Yes
Column lids	Stainless steel 316L	No
Distributor	Polypropylene	Yes
Bed support	Stainless steel 316L or polyethylene	Yes
Chromaflow nozzle	Polypropylene, stainless steel 316L, PEEK 450 G	Yes
Seals	EPDM or FEP encapsulated silicone	Yes
Stand	Stainless steel 316L	No

EPDM = ethylene propylene diene, FEP = fluoroethenopropene, PEEK = polyetherether ketone

Table 3. Chemical resistance of materials used in Chromaflow columns (60 days)

Chemical	Acrylic	SS 316L	EPDM	FEP	PEEK 450 G	PE	PP
Acetic acid 1.7 M	+	+	+	+	+	+	+
EtOH 20% ¹	+	+	+	+	+	+	+
EtOH 40%	-	+	+	+	+	(+)	+
Ethylene glycol 50%	+	+	+	+	+	+	+
Formaldehyde 1.7 M	+	+	+	+	+	+	+
Formic acid 10%	(+)	+	+	+	+	+	+
Glycerol 100%	+	+	+	+	+	+	+
Hydrochloric acid 0.1 M	+	-	+	+	+	+	+
Isopropyl alcohol 30%	-	+	+	+	+	(+)	+
Nitric acid 0.1 M	+	+	+	+	+	(+)	+
Phosphoric acid 25%	+	(+)	+	+	+	+	+
Sodium chloride 0.5 M	+	+ ²	+	+	+	+	+
Sodium hydroxide 2 M ³	+	+	+	+	+	+	+
Trifluoroacetic acid 0.1%	(+)	+	+	+	+	+	+
Triton™ X-100 100%	+	+	+	+	+	+	+
Urea 8 M	+	+	+	+	+	+	+

+ Resistant (+) Limited resistance - Not recommended

¹ Do not expose acrylic to concentrations of ethanol greater than 20%. Do not exceed the following parameters during storage: 5 yr, 23°C, 0.5 bar g.

² NaCl can cause corrosion on stainless steel at pH <5. Do not use NaCl in storage solutions. Rinse with at least 5 CV of clean water after use with NaCl.

³ Maximum exposure 4 h.

SS=stainless steel, EPDM=ethylene propylene diene, FEP=fluoroethenepropene, PEEK=polyetherether ketone, PE=polyethylene, PP=polypropylene.

Sanitizing Chromaflow columns

The design of Chromaflow columns facilitates cleaning-in-place. Below is a recommended cleaning protocol suitable for most applications.

1. Circulate 1.5 CV of 20% acetic acid at a low flow velocity (60 cm/h) for 15 min, upward flow. Then reverse the flow for 15 min.
2. Repeat this procedure with 1.0 M NaOH.
3. Following step 2, slowly circulate 1.0 M NaOH in the column for 60 min.
4. Re-equilibrate the column with a storing or starting buffer.

Chromaflow Packing stations

Chromaflow Packing stations make column priming and packing a simple operation, reducing the operator's time to a minimum. The packing stations consist of a control panel with pumps and valves fitted underneath (Fig 5). Valves and diaphragm pumps are actuated pneumatically from the control panel. As they are brought into operation indicators on the control panel display the relevant flow paths. For operation, packing stations only require a supply of compressed air. To select an appropriate packing station for your column and media, refer to Tables 4 and 5.



Fig 5. Chromaflow Packing station Pack 100.

Table 4. Specifications of Chromaflow packing stations

Designation*	Pump	Pump flow capacity (l/min)	Req. air supply (m ³ /min)	Inlet piping/outlet i.d. (mm)	TC connections (mm)	Weight, dry (kg)	Size W x H x D (mm)
Pack 50	Tapflo™ T53	10–50	0.5	22.1/22.1	50.5	115	810 × 1175 × 715
Pack 100	Tapflo T103	30–100	1.0	34.8/22.1	50.5	130	810 × 1175 × 715

* Packing stations, Pack 200 and Pack 400 with pump flow capacities of 60 to 200 l/min and 100 to 400 l/min are available as custom orders.

Table 5. Approximate packing flow rates for different media at two different bed heights

Column diameter (mm)		400				600				800				1000			
Bed height (mm)		150		300		150		300		150		300		150		300	
Flow		cm/h	l/min	cm/h	l/min	cm/h	l/min	cm/h	l/min	cm/h	l/min	cm/h	l/min	cm/h	l/min	cm/h	l/min
Sephacose™																	
Fast Flow media		500	11	250	5.5	500	24	250	12	500	42	250	21	500	66	250	33
Sephacose																	
Big Beads media		1600	34	1200	25	1600	75	1200	57	1600	134	1200	101	1600	209	1200	157

What else do I need?

The column

The columns are supplied ready for use and are equipped with adjustable feet. Castors can be ordered separately for columns up to 1000 mm in diameter.

Isolating the column after packing

We recommend using sanitary stainless steel valves (of the appropriate inner diameter) on the mobile phase to prevent contamination of the packed bed. For storage purposes, blind flanges with a clamp and gasket can be used to seal off the column.

Connecting the column to your system and packing station

Clamps and gaskets of suitable size are required to connect the sanitary flanged inlet/outlet to either valves or tubing of the same type. Preflanged tubing is also available.

Assembly or disassembly of the column

An adequate sized wrench is needed for assembly or disassembly of the column. A hoist is needed to remove the adapter or top lid from the column.

Spare parts to keep on site

It is recommended that nozzle seals, column seals, and column bed support kits are kept as spare parts.

Useful accessories

Safety valve: Precalibrated valve which releases pressure if the calibrated value is exceeded. Recommended to install on the mobile phase inlet if no other pressure sensor is included in the chromatography system. The T-junction, clamps and gaskets must be ordered separately.

Pressure sensor: The sensor is installed inline, preferably on the mobile phase inlet. Clamps and gaskets have to be ordered separately.

Ordering information

Columns

Chromaflo columns with acrylic tubes	Bed support 10 mm SS sinter	Bed support 20 mm SS sinter	Bed support 20 mm PE sinter
<i>I.d. 400 mm Man. nozzle</i>			
Stroke length 100-300	18-1150-40	18-1159-40	18-1161-40
Stroke length 200-400	18-1157-42	18-1159-42	18-1161-42
Stroke length 300-500	18-1157-44	18-1159-44	18-1161-44
<i>I.d. 400 mm Auto. nozzle</i>			
Stroke length 100-300	18-1157-41	18-1159-41	18-1161-41
Stroke length 200-400	18-1157-43	18-1159-43	18-1161-43
Stroke length 300-500	18-1157-45	18-1159-45	18-1161-45
<i>I.d. 400 mm SFP* Man. nozzle</i>			
Stroke length 100-300	18-1170-53	18-1176-12	11-0011-85
Stroke length 200-400	11-0011-80	11-0011-83	11-0011-86
Stroke length 300-500	11-0011-82	11-0011-84	11-0011-87
<i>I.d. 400 mm SFP Auto. nozzle</i>			
Stroke length 100-300	11-0011-89	11-0011-91	11-0011-94
Stroke length 200-400	11-0011-88	11-0011-92	11-0011-95
Stroke length 300-500	11-0011-90	11-0011-93	11-0011-96
<i>I.d. 600 mm Man. nozzle</i>			
Stroke length 100-300	18-1150-60	18-1159-60	18-1161-60
Stroke length 200-400	18-1157-62	18-1159-62	18-1161-62
Stroke length 300-500	18-1157-64	18-1159-64	18-1161-64
<i>I.d. 600 mm Auto. nozzle</i>			
Stroke length 100-300	18-1157-61	18-1159-61	18-1161-61
Stroke length 200-400	18-1157-63	18-1159-63	18-1161-63
Stroke length 300-500	18-1157-65	18-1159-65	18-1161-65
<i>I.d. 800 mm Man. nozzle</i>			
Stroke length 100-300	18-1150-80	18-1159-80	18-1161-80
Stroke length 200-400	18-1157-82	18-1159-82	18-1161-82
Stroke length 300-500	18-1157-84	18-1159-84	18-1161-84
<i>I.d. 800 mm Auto. nozzle</i>			
Stroke length 100-300	18-1157-81	18-1159-81	18-1161-81
Stroke length 200-400	18-1157-83	18-1159-83	18-1161-83
Stroke length 300-500	18-1157-85	18-1159-85	18-1161-85
<i>I.d. 1000 mm Man. nozzle</i>			
Stroke length 100-300	18-1150-10	18-1160-10	18-1162-10
Stroke length 200-400	18-1158-12	18-1160-12	18-1162-12
Stroke length 300-500	18-1158-14	18-1160-14	18-1162-14
<i>I.d. 1000 mm Auto. nozzle</i>			
Stroke length 100-300	18-1158-11	18-1160-11	18-1162-11
Stroke length 200-400	18-1158-13	18-1160-13	18-1162-13
Stroke length 300-500	18-1158-15	18-1160-15	18-1162-15

For column specifications other than listed in the table, please contact your local GE Healthcare representative.

* SFP = Small Flow Path on mobile phase, only available on 400 mm i.d. columns.

Packing stations

	Min (l/min)	Max (l/min)	Code No.
Pack 50	10	50	18-1163-74
Pack 100	30	100	18-1162-08
Pack 200	60	200	Custom order
Pack 400	100	400	Custom order

Accessories

Designation	Code No.	Designation	Code No.
Valves		Media stirrers	
4 port 2 way, i.d. 10 mm, 25 mm TC	18-1012-56	Media stirrer, 80 cm	18-1149-80
4 port 4 way, i.d. 10 mm, 25 mm TC	18-1012-57	Media stirrer, 150 cm	18-1149-81
3 port 2 way, i.d. 15 mm, 25 mm TC	44-5499-90	Connectors	
4 port 4 way, i.d. 20 mm, 51 mm TC	44-2302-01	i.d. 10, 25 mm TC-3/4"-20 UNF threaded	18-1012-68
3 port 2 way, i.d. 22 mm, 51 mm TC	44-1583-01	i.d. 10, 25 mm TC-i.d. 14, 51 mm TC	18-1027-25
3 port 2 way, i.d. 35 mm, 51 mm TC	44-5494-65	i.d. 14, 51 mm TC-i.d. 22, 51 mm TC	18-1027-26
Valve sealing washer	18-1128-69	Chromaflow Nozzle control unit	18-1164-61
<i>Fits 10 mm 2- and 4-way valves</i>		Chromaflow Nozzle pipings	
PVC tubing with sanitary fitting 25 mm TC		Chromaflow Nozzle piping 400 1/2"	18-1172-01
i.d. 10 mm, 900 mm	18-1012-62	Chromaflow Nozzle piping 400 3/4"	18-1172-00
i.d. 10 mm, 1400 mm	18-1012-63	Chromaflow Nozzle piping 400 1"	18-1171-99
i.d. 10 mm, 1700 mm	18-1012-64	Chromaflow Nozzle piping 600 1/2"	18-1172-06
i.d. 10 mm, 2000 mm	18-1012-87	Chromaflow Nozzle piping 600 3/4"	18-1172-05
i.d. 14 mm, 750 mm	18-1027-28	Chromaflow Nozzle piping 600 1"	18-1172-04
i.d. 14 mm, 1800 mm	18-1027-29	Chromaflow Nozzle piping 800 1/2"	18-1171-94
PVC tubing with sanitary fitting 51 mm TC		Chromaflow Nozzle piping 800 3/4"	18-1171-93
i.d. 22 mm, 900 mm	44-1616-09	Chromaflow Nozzle piping 800 1"	18-1171-92
i.d. 22 mm, 1400 mm	44-1616-08	Chromaflow Nozzle piping 1000 1/2"	18-1172-09
i.d. 22 mm, 2000 mm	44-1616-07	Chromaflow Nozzle piping 1000 3/4"	18-1172-08
i.d. 22 mm, 4000 mm	44-1616-06	Chromaflow Nozzle piping 1000 1"	18-1172-07
Clamp gasket			
25 mm i.d., 10 mm	18-1035-79		
25 mm i.d., 12 mm	18-0200-00		
51 mm i.d., 22 mm	44-7133-01		
51 mm i.d., 38 mm	44-0515-01		
Clamp 25 mm	18-1001-31		
Clamp 51 mm	44-7134-01		
Blind flange 25 mm incl. gasket	18-1001-25		
Blind flange 51 mm incl. gasket	44-7135-01		
Safety valve, 3 bar, 51 mm TC	18-5738-01		
Safety valve, 5 bar, 51 mm TC	44-5498-97		
T-junction i.d., 10 mm, 2x25 mm TC, 1x51 mm TC	18-1003-63		
Castors, assembly kit 400-600	18-1171-51		
Castors, assembly kit 800-1000	18-1171-52		
<i>The kit contains a complete set of wheels, fasteners and adapters for a column.</i>			
Pressure sensor i.d. 10 mm, 25 mm TC	44-0507-02		
Pressure sensor i.d. 22 mm, 51 mm TC	44-0507-03		

www.gehealthcare.com/protein-purification-bioprocess

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imagination at work

nProtein A Sepharose 4 Fast Flow

nProtein A Sepharose™ 4 Fast Flow is native protein A coupled to Sepharose 4 Fast Flow. It has nearly twice the total IgG binding capacity of Protein A Sepharose CL-4B, and is the ideal adsorbent for recovery and purification of monoclonal antibodies from cell culture at both laboratory and process scale.

nProtein A Sepharose 4 Fast Flow has been developed and tested in cooperation with leading manufacturers of purified monoclonal antibody products, and is used in routine commercial production.

nProtein A Sepharose 4 Fast Flow replaces Amersham Biosciences' former Protein A Sepharose 4 Fast Flow.

Features

- Low leakage of protein A
- Used in large scale FDA approved processes
- Manufactured without using any animal-derived components

The product

Native protein A has a molecular weight of 42 000 daltons, and a structure consisting of several regions (see Fig. 1). Five of these (E, D, A, B and C) show strong specific affinity for the Fc part of IgG, leaving the antigen combining sites within the regions free (1, 2, 3). One molecule of immobilized protein A binds at least two molecules of IgG.

Staphylococcal Protein A

S	E	D	A	B	C	Xr	Xc
---	---	---	---	---	---	----	----

Fig 1. Schematic drawing of regions encoded by the gene for *Staphylococcal* protein A. S is the signal sequence. E, D, A, B and C are the homologous repetitive immunoglobulin binding regions. Xr and Xc are C-terminal located, non-immunoglobulin binding regions thought to be responsible for the binding of Protein A to the bacterial cell (4).



Amersham Biosciences' native protein A is produced by fermenting a selected strain of *Staphylococcus aureus*. The purified protein is coupled to Sepharose 4 Fast Flow by the cyanogen bromide technique, giving a highly stable medium with minimal non-specific adsorption. nProtein A Sepharose 4 Fast Flow is manufactured without using any animal-derived components.

The swollen medium has a protein A content of approximately 6 mg/ml drained medium. The total binding capacity for human IgG is approximately 35 mg/ml drained medium.

Sepharose 4 Fast Flow is a highly cross-linked, 4% agarose derivative with impressive kinetics, leading to excellent chromatographic qualities in the immobilized affinity adsorbent. Its rigidity also makes it ideal for process scale applications. nProtein A Sepharose 4 Fast Flow is particularly suitable for recovery and purification of monoclonal antibodies from cell culture supernatants. The rigidity and high degree of substitution of the Sepharose 4 Fast Flow matrix enables the rapid processing of large volumes of dilute cell culture fluid.

Stability

nProtein A Sepharose 4 Fast Flow has high chemical and mechanical stability. It withstands high concentrations of hydrogen bond disrupting agents such as urea, guanidine hydrochloride and sodium thiocyanate. It has high thermal stability, but is not autoclavable. The characteristics of the product are summarized in Table 1.

Table 1. Characteristics of nProtein A Sepharose 4 Fast Flow

Ligand	native Staphylococcal protein A
Degree of substitution	approx. 6 mg native protein A/ml drained medium
Ligand coupling method	cyanogen bromide activation
Dynamic binding capacity*	min 20 mg human IgG/ml drained medium
Matrix	highly cross-linked 4% agarose
Average particle size	90 µm (45–165 mm)
Chemical stability	no significant change in chromatographic performance after 1 week storage using 8 M urea, 6 M guanidine-HCl, 2% benzyl alcohol or 20% ethanol
pH stability**	
Working	2–9
Long term	3–9
Short term	2–10
Max linear flow rate	1300 cm/h at 25 °C, XK 16/20 column, bed height 5 cm
Max operating back pressure	0.1 MPa (1 bar, 14 psi)
Sanitization	wash the packed column with 2% hibitane/20% ethanol or 70% ethanol
Storage	20% ethanol at +4 to +8 °C

* The binding capacity was determined at a linear flow rate of 100 cm/h, column: 7.5 x 50 mm, sample volume: 250 µl, sample concentration: 1 mg human IgG/ml

** Complete data on the stability of protein A as a function of pH are not available. The ranges given are estimates based on our knowledge and experience. Please note the following:

pH stability, long term refers to the pH interval where the medium is stable over a long period of time without adverse effects on its subsequent chromatographic performance.

pH stability, short term refers to the pH interval for regeneration, cleaning-in-place and sanitization procedures

pH below 3 is sometimes required to elute strongly bound Ig's. However, protein ligands may hydrolyse at very low pH

Process scale use

a) Columns

Columns recommended for nProtein A Sepharose 4 Fast Flow are shown in Table 2.

Table 2. Recommended Amersham Biosciences columns for nProtein A Sepharose 4 Fast Flow.

Column	Bed height	Medium volume
XK Column 50/30 Fast Flow*	5–15 cm	100–300 ml
BPG™ 100/500		Up to 2.4 l

* These are columns fitted with a special Fast Flow adaptor to increase throughput.

When packing the medium at a 5 cm bed height, the recommended packing flow velocity is at least 700 cm/h, and at a 15 cm bed height at least 300 cm/h. The working flow velocity should not exceed 80% of the packing flow velocity. As a guide pressure/flow velocity curves for the Sepharose 4 Fast Flow base matrix packed in XK 50/30 Fast Flow and BP 113 columns are shown in Figure 2.

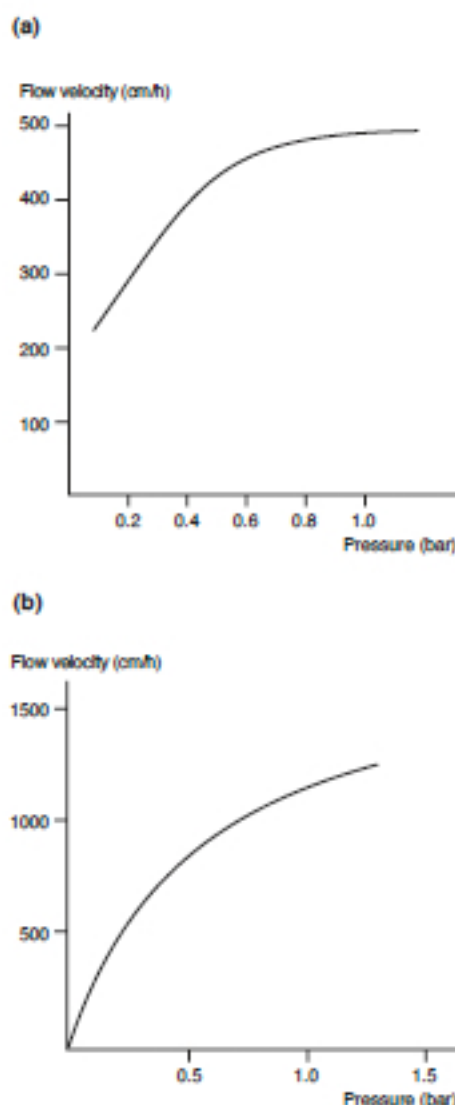


Fig 2. Pressure/flow velocity curve for Sepharose 4 Fast Flow in XK 50/30, bed height 15 cm (a) and BP 113, bed height 5 cm (b); mobile phase H₂O. (Work from Amersham Biosciences AB).

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Max operating back pressure	0.1 MPa (1 bar, 14 psi)
Sanitization	wash the packed column with 2% hibitane/20% ethanol or 70% ethanol
Storage	20% ethanol at +4 to +8 °C

* The binding capacity was determined at a linear flow rate of 100 cm/h, column: 7.5 x 50 mm, sample volume: 250 µl, sample concentration: 1 mg human IgG/ml

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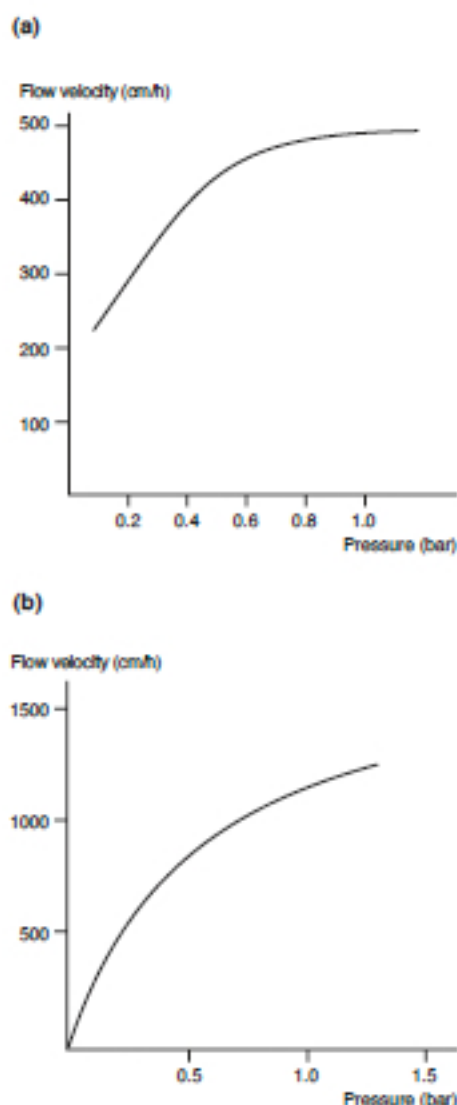


Fig 2. Pressure/flow velocity curve for Sepharose 4 Fast Flow in XK 50/30, bed height 15 cm (a) and BP 113, bed height 5 cm (b); mobile phase H₂O. (Work from Amersham Biosciences AB).

b) Dynamic capacity

The dynamic capacity of chromatographic adsorbents is a function of the flow velocity used for loading samples, and increases with decreasing flow velocity. Furthermore, individual antibodies differ in their affinity to protein A. To obtain an optimal purification scheme with respect to capacity and time, it is necessary to first determine the capacity for the specific antibody to be purified over a range of different flow velocities (see the example in Fig. 3). Once this is known it is then possible to control the flow velocity during the loading phase to achieve maximum binding of the antibody in minimum time. In practice, this means initially loading the sample at a high flow velocity (e.g. 300 cm/h) and reducing the flow velocity successively with increasing sample load.

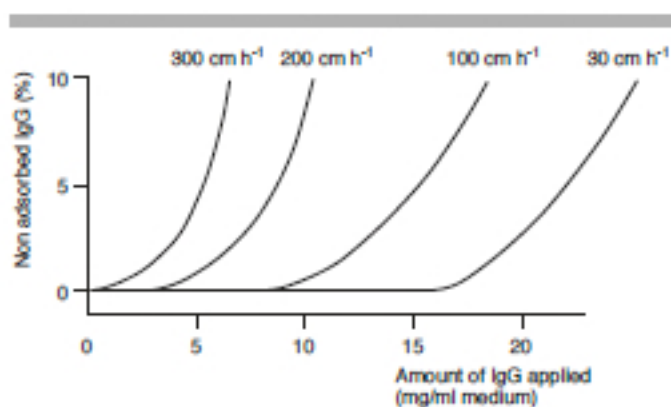


Fig 3. One example of how the capacity for human IgG depends on the flow velocity with nProtein A Sepharose 4 Fast Flow. The non-adsorbed IgG (%) was measured as a function of the amount applied to the column at 4 different flow velocities, 300, 200, 100 and 30 cm/h. Concentration of the applied sample: 0.33 mg IgG/ml. Column: HR 5/5. Buffer system: 0.1 M Na_2HPO_4 , pH 7.0. (Work from Amersham Biosciences AB).

c) Operation

nProtein A Sepharose 4 Fast Flow is supplied in suspension in 20% ethanol.

1. After packing, wash the medium bed with at least three column volumes of starting buffer to remove preservative.
2. Note the following points when loading the sample:
 - The sample pH should be the same as the starting buffer pH.
 - The sample should be filtered through a 0.22 – 0.45 μm filter. (This prolongs the working life of the medium).
3. After loading the sample, wash the medium with starting buffer until the base line is stable.
4. When eluting the sample, reverse the direction of flow.

d) Process Hygiene

Good process hygiene ensures the safety and integrity of the final product by removing or controlling any unwanted substances which might be present or generated in the raw material, or derived from the purification system itself. In practice, process hygiene of most affinity media usually means reduction of product contamination by sanitization, followed by a cleaning step.

Sanitization

Sanitization is the reduction of microbial populations on the medium. Two suggested alternative protocols are:

- i) Equilibrate with a buffer consisting of 2% hibitane digluconate and 20% ethanol.
 - ii) Allow to stand for 6 hours.
 - iii) Wash with sterile buffer.
- or
- i) Equilibrate with 70% ethanol.
 - ii) Allow to stand for 12 hours.
 - iii) Wash with sterile buffer.

Cleaning

The general recommendation for cleaning nProtein A Sepharose 4 Fast Flow is to use a mixture of 50 mM NaOH and 1 M NaCl. As an alternative cleaning protocol 6 M guanidine hydrochloride can be used. Phosphoric acid (100 mM) has also been used for cleaning. To remove hydrophobically bound substances a solution of non-ionic detergent or ethanol is recommended.

e) Regeneration

After each separation cycle, regenerate the medium bed by washing with approximately 3 column volumes of 0.1 M citrate buffer, pH 3 until the base line is stable.

f) Storage

For longer periods of storage, keep nProtein A Sepharose 4 Fast Flow in a suitable bacteriostat, e.g. 20% ethanol, at 4–8 °C. The medium must not be frozen.

Applications

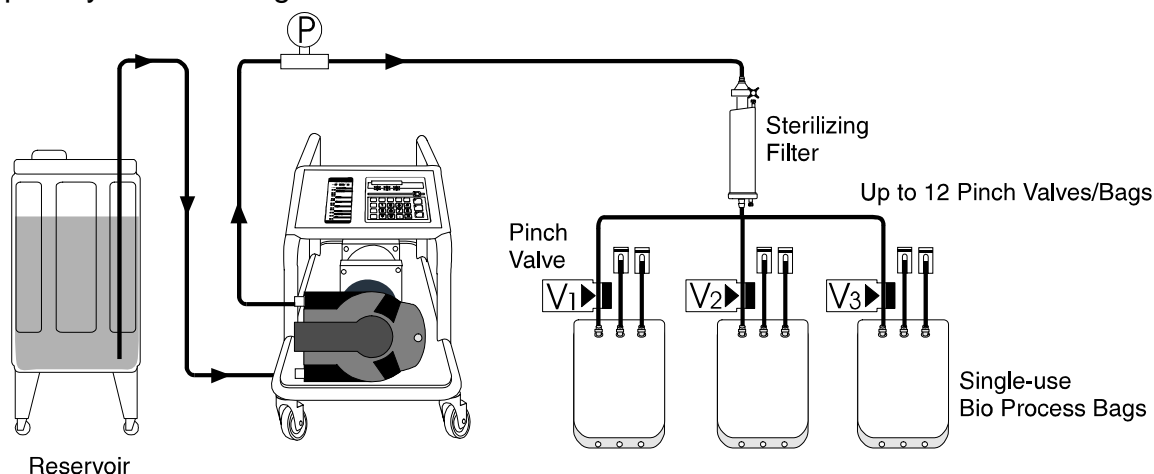
The most important application area for nProtein A Sepharose 4 Fast Flow is the purification of monoclonal antibodies from cell culture (5, 6). High IgG capacity and high flow velocities make the medium ideal for both laboratory and process scale separations.

There is a natural diversity between the different subclasses of IgG and even within subclasses. Therefore the binding and elution system must be optimized for every monoclonal antibody to be purified.

Automated, Aseptic Transfer of Liquids into Multiple, Single-use Storage Bags

Summary:

The Fill Master aseptically transfers solution into multiple, plastic storage bags. The Fill Master controls up to twelve, pneumatically operated tube pinch valves to direct the liquid flow from the reservoir into sterile storage bags. Only the internal tube walls and the inside bag surfaces are in contact with the liquid. The high-accuracy, low-shear peristaltic pump action provides gentle and reproducible bag filling. In the programmable, volume dispensing mode, the Fill Master meters a user-defined volume of liquid, then automatically switches to the next empty storage bag to be filled. Up to 12 storage bags can be serially filled in this fashion. Once filled, the bags can be aseptically sealed using a sterile tube welder.



Features:

There are several Fill Master models to choose from. For example, the Fill Master 104B peristaltic pump head (max. pump rate is 14.6 liters/min with #184 Silicone tubing) allows for a continuous tube connection to be made between the reservoir and the storage bag manifold. A typical sterile fluid handling bag manifold, which may include multiple storage bags, as well as integral tubing, QC bags, sterilizing filter and connectors, are available pre-sterilized (i.e. gamma irradiated). Contact SciLog for info.

When ordering a sterile fluid handling bag manifold, the size and material of the integral tubing must be specified. The Fill Master 104B peristaltic pump head can accommodate the following tubing sizes: #26, 6.4 mm ID (0.15 to 2.60 liters/min); #73, 9.6mm ID (0.31 to 5.94 liters/min); #82, 12.7 mm ID (0.53 to 9.25 liters/min) and #184, 15.9 mm ID (0.80 to 14.50 liters/min) A range of tube materials can be used: Silicone, Pharmed, PVC and C-Flex (heat sealable). Other Fill Master models accommodate additional sizes.

An optional, disposable pressure transmitter can be placed in front of the in-line sterilizing filter to monitor filter backpressure. With the pressure transmitter connected to the Fill Master, excessive pressure build-up as well as associated leaks and bag failures are prevented. The Fill Master will stop all pumping action when a user-defined safe pressure limit is exceeded.

Automated Bag Filling Operation: *Fill Master Metering Program*

The Fill Master Volume-Flow mode (Mode 30) allows you to enter (in "EDIT") and store an automated metering program. The following is a simple program to fill three, 20 liter storage bags. Change the RATE and TIME program steps to suit your storage bag volume. Add additional "RUN" program blocks to increase the number of bags (up to 12) you want to fill.

000	START	<i>The following program steps have been entered in Mode 30:</i>
001	CW	<i>Motor Runs Clock-wise</i>
002	RUN	<i>Motor is turned "ON"</i>
003	V 100000	<i>Pinch Valve V1 is Energized, other V-valves are De-energized</i>
004	RATE: 5.0L/min	<i>Pump Rate 5 liters per minute</i>
005	TIME: 00:04:00	<i>Pump Runs 4 minutes, Bag #1 is filled with 20 Liters</i>
006	STOP	<i>Pump "Off"</i>
007	V 020000	<i>Pinch Valve V2 is Energized, other V-valve are De-energized</i>
008	TIME: 00:00:02	<i>2 Second Time delay</i>
009	RUN	<i>Pump "ON"</i>
010	RATE: 5.0 L/min	<i>Pump Rate 5 liters per minute</i>
011	TIME: 00:04:00	<i>Pump Runs 4 Minutes, Bag #2 is filled with 20 Liters</i>
012	STOP	<i>Pump "Off"</i>
013	V 003000	<i>Pinch Valve V3 is Energized, other V-valves are De-energized</i>
014	TIME: 00:00:02	<i>2 Second Time Delay</i>
015	RUN	<i>Pump "ON"</i>
016	RATE: 5.0 L/min	<i>Pump Rate 5.0 liters per minute</i>
017	TIME: 00:04:00	<i>Pump Runs 4 Minutes, Bag #3 is filled with 20 Liters</i>
018	STOP	<i>Pump "Off"</i>
019	V 000000	<i>All V-Valves are De-energized</i>
020	COUNT: 1	<i>The Program Steps 000 to 020 are executed once</i>
021	END	

ORDERING INFORMATION:

SciLog Customer Service: 1-800-955-1993

Catalog #: Description:

- 800-104BFILL** **Fill Master 104B mounted with a Watson-Marlow 620R peristaltic pump head**, 0.5 HP motor; 90VDC; 250 RPM max.; 7.8: 1 Speed Reducer. The 620R peristaltic pump head has two (2) pump rollers and accommodates continuous pump tubing of the following sizes: 6.4mm ID (#26), 0.15 to 2.60 L/M; 9.6mm ID (#73) 0.31 to 5.94 L/M; 12.7mm ID (#82), 0.53 to 9.25 L/M; and 15.9mm ID (#184), 0.80 to 14.5 L/M, wall thickness is 3.2mm (0.125") for all tube sizes
- 800-450** **Multiple-Valve Controller:** Remote control of twelve (12) electrically actuated air flow valves (Clippard) for automated pneumatic operation of twelve (12) pinch valves or sanitary diaphragm valves. Fully programmable from the Fill Master via dedicated serial port or manual control from front panel of the multi-Valve Box. Optional inputs for valve position sensors.
- 934-VALVE** **Tubing Pinch Valve:** Specify Tubing OD: 0.125", 0.250", 0.375", 0.50", 0.75", and wall thickness. The valve is pneumatically actuated. Ideal for maintaining sterility, only tubing comes in contact with your process solution. Requires a Multi-Valve Controller for actuation and control. The Multi-Valve Controller is fully programmable from the Fill Master via dedicated serial port or manual control from front panel of multi-Valve Box. Optional inputs for valve position sensors.



Labtainer™ System

BioProcess Container™ Systems for small volume liquid handling applications in bioresearch and biopharma production.

Animal Derived Component Free (ADCF™) Film • Sizes range from 50 mL–50 L

.....

Applications:

- Collection, storage, and transport of sterile liquids
- Delivery of media to small-scale biotechnology production systems
- Formulation and filling of sterile media, buffers, and other process liquids
- Chromatography feed and fraction collection
- Bioreactor and fermentation feed and harvest
- Transportation and storage of bulk intermediate product
- Freezing/thawing, heat inactivation, and irradiation of product

HyQ®CX5-14 Film

- Regulatory friendly due to ADCF status and low extractables
- Improved shelf life of media due to superior barrier properties
- Scalability from 50 mL–2500 L in same film

Flexible and Secure Containers

- Save storage space
- Safer than carboys
- Easy to handle (handling systems available)

Single-Use; Arrive Sterile and Ready-to-use

- No cleaning or sterilization
- Minimize validation requirements
- Labor and cost saving

Range of Standard Products

- Integrate with most industry standard connection systems



▼ Ordering Information

▼ **Consumable** (single-use, reordered on demand)

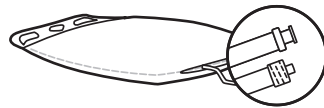


2-D, Hanging Pillow

2 ports, end dispense

Line 1	1/4" (6.4 mm) Male LL (fitting directly attached to BPC)
Line 2	1/4" (6.4 mm) Female LL (fitting directly attached to BPC)

Single-pk Part#	10-pk Part#	Size
SH30657.01	SH30657.11	50 mL
SH30657.02	SH30657.12	100 mL
SH30657.03	SH30657.13	250 mL
SH30657.04	SH30657.14	500 mL
SH30657.05	SH30657.15	1000 mL
SH30657.06	SH30657.16	2000 mL



2-D, Hanging Pillow

2 ports, end dispense

Line 1	1/8" (3.2 mm) Male LL (tube length: 12" / 30.5 cm)
Line 2	1/8" (3.2 mm) Female LL (tube length: 12" / 30.5 cm)

Single-pk Part#	10-pk Part#	Size
SH30658.01	SH30658.11	50 mL
SH30658.02	SH30658.12	100 mL
SH30658.03	SH30658.13	250 mL
SH30658.04	SH30658.14	500 mL
SH30658.05	SH30658.15	1000 mL
SH30658.06	SH30658.16	2000 mL

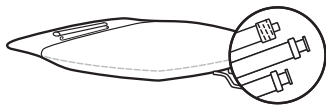


2-D, Hanging Pillow

2 ports, end dispense

Line 1	1/8" (3.2 mm) Female LL (tube length: 12" / 30.5 cm)
Line 2	1/4" (6.4 mm) QC Insert (fitting directly attached to BPC)

Single-pk Part#	10-pk Part#	Size
SH30662.01	SH30662.11	50 mL
SH30662.02	SH30662.12	100 mL
SH30662.03	SH30662.13	250 mL
SH30662.04	SH30662.14	500 mL
SH30662.05	SH30662.15	1000 mL
SH30662.06	SH30662.16	2000 mL

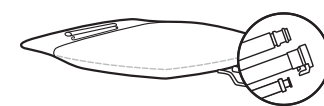


2-D, Hanging Pillow

3 ports, end dispense

Line 1	1/4" (6.4 mm) Male LL (tube length: 12" / 30.4 cm)
Line 2	1/4" (6.4 mm) Female LL (tube length: 12" / 30.4 cm)
Line 3	1/8" (3.2 mm) Female LL (tube length: 12" / 30.4 cm)

Single-pk Part#	Size
SH30713.01	5 L
SH30713.02	10 L
SH30713.03	20 L
SH30713.04	50 L

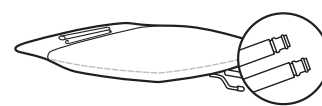


2-D, Hanging Pillow

3 ports, end dispense

Line 1	3/8" (9.5 mm) QC Insert (tube length: 24" / 61 cm)
Line 2	3/8" (9.5 mm) QC Body (tube length: 24" / 61 cm)
Line 3	1/8" (3.2 mm) Female LL (tube length: 24" / 61 cm)

Single-pk Part#	Size
SH30712.01	5 L
SH30712.02	10 L
SH30712.03	20 L
SH30712.04	50 L

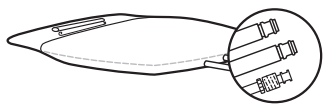


2-D, Hanging Pillow

3 ports, end dispense

Line 1	3/8" (9.5 mm) QC Insert (tube length: 12" / 30.4 cm)
Line 2	3/8" (9.5 mm) QC Insert (tube length: 12" / 30.4 cm)
Line 3	1/4" (6.4 mm) Plugged

Single-pk Part#	Size
SH30714.01	5 L
SH30714.02	10 L
SH30714.03	20 L
SH30714.04	50 L



2-D, Hanging Pillow

3 ports, end dispense

Line 1	3/8" (9.5 mm) QC Insert (fitting directly attached to BPC)
Line 2	3/8" (9.5 mm) QC Insert (fitting directly attached to BPC)
Line 3	Injection Port (fitting directly attached to BPC)

Single-pk Part#	Size
SH30709.01	5 L
SH30709.02	10 L
SH30709.03	20 L
SH30709.04	50 L

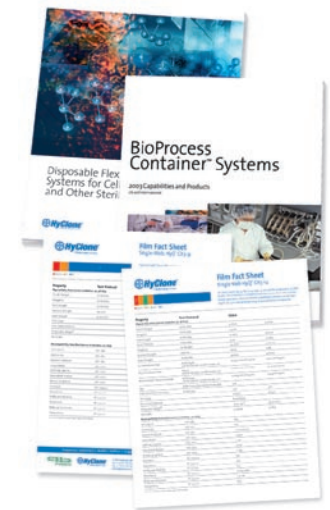
- > All end fittings are capped or plugged.
- > All tubing lines are C-Flex® and provided with clamps. (C-Flex is a registered trademark of Consolidated Polymer Technologies.)
- > LL = Luer Lock
- > QC = Quick Connect

▼ Accessories

- Hanging Rack—assists in the handling of product.
 - Totes/Tote Rack—assists in the handling of product.
 - Adapter Tube Sets—extend functionality of product by using adapter tube sets.
- Additional information available on request.

▼ Technical Information

Additional technical information (HyQ®CX5-14 fact sheet, film white paper, and the BPC Capabilities and Products Brochure) is available upon request. Please contact your HyClone customer service representative.



▼ Customization

For orders that require a customized solution, please contact your HyClone sales representative to initiate a Product Brief, defining your intended application and requirements.



bioprocess containers • media • buffers • reagents • serum-free media • FBS replacements • sera



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QUALITY BIORESOURCES, INC
1015 N. AUSTIN STREET
SEGUIN, TEXAS 78155
(830) 372-4797

CUSTOMER QUOTATION

DATE	QUOTE NO.
4/2/2009	9002-1655

NAME / ADDRESS
UNIVERSITY OF PENNSYLVANIA

SHIP TO
Kevin Hsu

ITEM	QTY	DESCRIPTION	SPECIAL QUOTE
CUSTOM	225,000	MONOCLONAL ANTIBODY, LYOPHILIZED, 1ML PER VIAL, CLEAR GLASS SERUM VIAL, BUTYL RUBBER STOPPER, NATURAL ALUMINUM CRIMP, PACKAGED IN SHRINK-WRAPPED TRAYS	225,000
CUSTOM	225,000	OR MONOCLONAL ANTIBODY, LYOPHILIZED, 1ML PER VIAL, CLEAR GLASS SERUM VIAL, BUTYL RUBBER STOPPER, NATURAL ALUMINUM CRIMP, LABELED, PACKAGED IN SHRINK-WRAPPED TRAYS	270,000

PAYMENT TERMS: NET 30 DAYS

SHIPMENT TERMS: FOB SEGUIN, TEXAS

QUOTED PRICES ARE VALID FOR SIXTY (60) DAYS FROM QUOTATION DATE SHOWN ABOVE.
PLEASE REFER TO QUOTATION NUMBER ON ALL ORDERS.



B I O - P H A R M

CIP Washers

Clean-In-Place Systems

Sani-Matic Clean-In-Place Systems for the Bio-Pharm industry are custom engineered to specific plant application and utility requirements to ensure effective and efficient cleaning of process equipment automatically.

Proper CIP design and sizing will not only ensure sufficient flow and pressure to remove residue adequately, and rinse thoroughly. Sani-Matic CIP designs will also save cycle time, reduce water and chemical usage, and minimize discharge and utility costs. Balancing all factors to create an optimum system is our goal. CIP Systems can be designed to recirculate or provide "once-through" cleaning, depending on the product residue. Multi-tank systems can provide additional benefits of faster turnaround time if cleaning processes are more frequent.

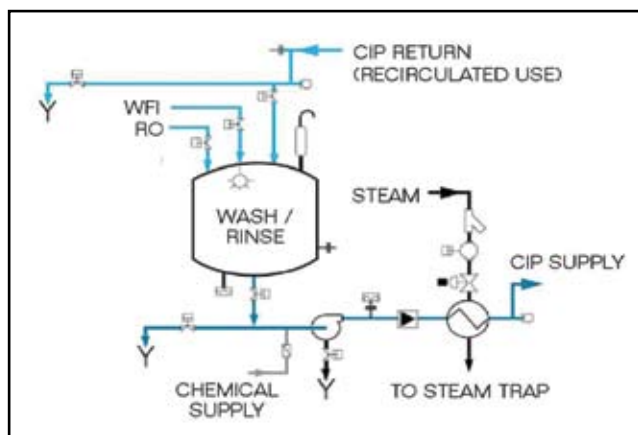
WHAT MAKES US DIFFERENT?

Sani-Matic has the expertise to engineer an effective solution for your cleaning application. Specialists in cleaning technology, the Sani-Matic team will provide valuable insight and guidance during your project from beginning to end. Developing a creative design concept based on decades of practical experience, we can ensure you are purchasing a system which is dependable and cost-effective for the long term. Sani-Matic has in-house programming staff and field technical service with the expertise to develop and optimize your cleaning cycles and integrate the CIP functions with your plant Process control systems. Because the Sani-Matic team understands the unique challenges of cleaning, we add value to your CIP projects.



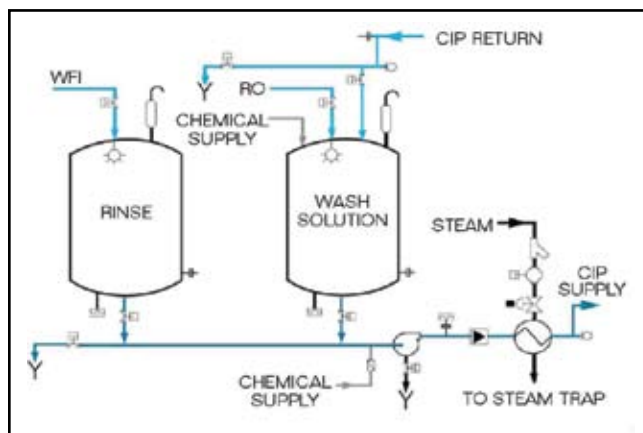
Our manufacturing facilities and processes are controlled and efficient, ensuring that your system is compliant and on-schedule. Project management and documentation is detailed and complete, saving you time and resources while achieving your project's budget and target start-up date.

One Tank Single-use System



- Single-use source of wash solution and rinse water
- Lower space requirement
- Portable or stationary design is available
- Once through or recirculated

Two Tank Detergent & Rinse System



- Permits once through or recirculated flow of wash solution
- Used where water utilities are limited
- Reduced wash cycle times

CIP DESIGN SIZING FACTORS

CIP system sizing is determined by dimensions of the vessels and pipelines to be cleaned.

Supply pump flow is determined by the vessel size and the largest pipeline diameter. Turbulent cleaning action requires 5-7 fps flow in lines. Proper cascading cleaning action by a sprayball is 3 gpm per ft of tank circumference.

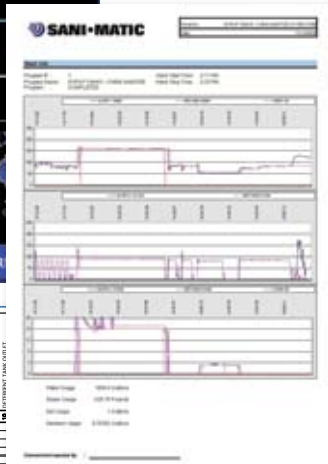
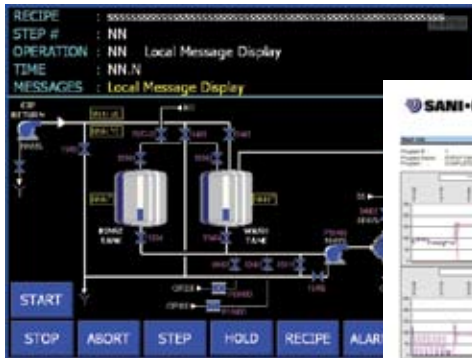
Pressure is determined by the spray device requirement (typically 25psi, plus any line loss).

Sizing the wash and rinse tank volume is determined by the pipeline holdup volume (gal per 100ft) and the available inlet water capacity and the estimated cleaning program time.

Tube OD	Tube ID	Volume Per 100'	Industry Minimum 5 ft/sec	Recommended 7 ft/sec	Maximum Gravity Flow thru Outlet
0.5"	0.37"	0.56 gal	2 GPM	3 GPM	
0.75"	0.62"	1.57 gal	5 GPM	7 GPM	
1.0"	0.87"	3.1 gal	10 GPM	13 GPM	
1.5"	1.37"	7.7 gal	23 GPM	32 GPM	35-40 GPM
2.0"	1.87"	14 gal	43 GPM	60 GPM	75-80 GPM
2.5"	2.37"	23 gal	69 GPM	96 GPM	115-120 GPM
3.0"	2.87"	34 gal	101 GPM	141 GPM	190-200 GPM
4.0"	3.834"	60 gal	180 GPM	252 GPM	250-275 GPM
6.0"	5.834"	139 gal	417 GPM	583 GPM	720 GPM

Controls

Easier/Faster to Validate



OPCODE NUMBER	DESCRIPTION	OPCODE NUMBER	DESCRIPTION
1	"PROGRAM END"	1	
2	"CIP PROGRAM START"	2	
3	"CIP PROGRAM END"	3	
4	"RINSE TO DRAIN"	4	
5	"RINSE TO DRAIN"	5	
6	"BURST PRE RINSE TO DRAIN"	6	
7	"DETERGENT WASH"	7	
8	"DETERGENT WASH"	8	
9	"CHASE RINSE TO DRAIN W/ DETERGENT"	9	
10	"CHASE RINSE TO DRAIN W/ ACID"	10	
11	"CHASE RINSE TO DRAIN W/ DETERGENT AND CONDUCTIVITY HOLD"	11	
12	"CHASE RINSE TO DRAIN W/ ACID AND CONDUCTIVITY HOLD"	12	
13	"CHEMICAL SANITISE"	13	
14	"CHEMICAL SANITISE"	14	
15	"PUMPBACK TO DRAIN"	15	
16	"PUMPBACK TO DRAIN"	16	
17	"PUMPBACK W/ DETERGENT RECOVERY"	17	
18	"PUMPBACK W/ ACID RECOVERY"	18	
19	"RINSE TO DRAIN"	19	
20	"RINSE TO DRAIN WITH RETURN CONDUCTIVITY HOLD"	20	
21	"RINSE TO DRAIN WITH RETURN CONDUCTIVITY HOLD"	21	
22	"RINSE TO DRAIN WITH RETURN CONDUCTIVITY HOLD"	22	
23	"RINSE TO DRAIN WITH RETURN CONDUCTIVITY HOLD"	23	
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100	"RINSE TO DRAIN WITH RETURN CONDUCTIVITY HOLD"	100	

Sani-Matic has in-house programmers and authorized UL panel shop who design, manufacture, pre-test, startup and support of all types of Control Systems for cleaning systems. Because the team specializes in cleaning applications, Sani-Matic has developed expertise and efficiencies that have advantages over other fabricators or process integrators. Sani-Matic has designed, manufactured and supported thousands of CIP systems and other cleaning related systems.

Understanding the unique aspects of an effective cleaning program, Sani-Matic developed a very flexible & easy-to-understand OP-Code Recipe Editor that allows the customer to manipulate the system hardware to optimize their cleaning programs. This can result shorter total cycle time, lower water & chemical usage, more precise control to setpoints and detailed alarms which reduce troubleshooting time.

Soon to be released, the new Sani-Trend Data Acquisition System collects and stores cleaning cycle data, events/alarms, and operator information onto a PC. Operating usage of water, chemical, and utilities may be calculated and trended. Sani-Trend reports are in easy to use Excel format, and provide reliable, secure information giving you valuable insight on your cleaning process.

UltraFlow

UltraFlow technical brochure available separately.



The Sani-Matic UltraFlow CIP is patented technology which uses an eductor, vortex air separation chamber and modulating valves to control the CIP supply and return flows. This unique CIP design successfully brings air & water back in the return flow, separates the air, keeping the supply pump primed. The UltraFlow uses much less water than traditional CIPs and is flexible to clean a wide variety of circuits.

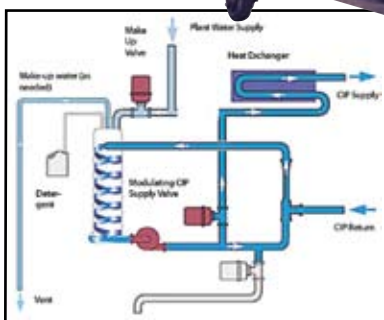
ADVANTAGES

- Reduce water usage
- Lower chemical consumption
- Eliminate installation costs
- Increase flexibility

THE IDEAL SOLUTION FOR:

- Vessels with low and/or small outlets
- Variable supply and return flow (1 to 100 GPM)
- Portable - Avoid investment in permanent supply & return lines
- Locations with limited/low water volume available
- Economical replacement for an existing or outdated CIP
- Installations where available floor space is limited

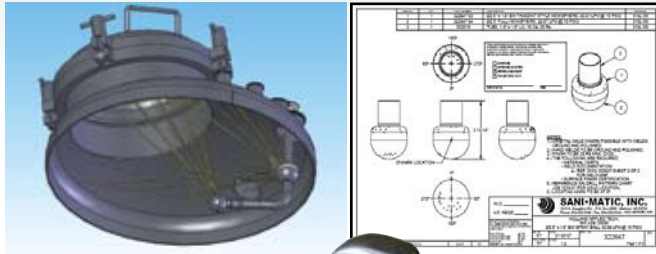
-548- Not appropriate for "once through" non-recirculated processes



CIP Features

Spray Devices

Custom Engineered and Precision Drilled



- Custom engineered in 3D
- Precision drilled
- Pass Riboflavin testing first time
- Documented for future replacement without re-validating

Sani-Matic designs and manufactures a complete range of sprayballs and associated solution tubes and tank fittings.

Utilizing the latest technology, Sani-Matic has engineered a method to model a process vessel in 3D and design the most effective spray device and drill pattern to ensure proper coverage of all ports and surfaces. With decades of experience in spray technology and Bio-Pharm CIP applications, the Sani-Matic team understands the spray dynamics required to ensure adequate flows, pressures and geometries will dependably clean your process equipment.

Sani-Matic provides complete documentation and ID marking for ease of validation and future replacement. Responsive service and reliable delivery make Sani-Matic the preferred supplier of Spray Devices in the market today.

Documentation

Faster & Easier Validation

- Operation and maintenance manuals
- Recommended spare parts list
- Instrument lists
- Instrumentation calibration procedures
- Performance data
- Material certificates
- Weld qualification and inspection records
- Inspection test results, reports and certificates
- ASME data
- Component catalog cut sheets
- As built assembly drawings
- As built process and instrumentation diagrams
- As built electrical drawings
- Annotated PLC ladder diagrams

OPTIONAL

- (FRS/FDS) Functional Design Specifications
- Control System Design Specification (HRS and SRS)
- (FAT) Factory Acceptance Test report
- (SAT) Site Acceptance Test document
- IQ/OQ installation and operation qualification
- Cleaning and passivation report
- Weld video record (Boroscope)

Sani-Matic personnel are active participants in the following organizations:

ISPE-International Society of Pharmaceutical Engineers

Co-developer & Co-leader of "Cleaning Technology" course

ASME-American Society of Mechanical Engineers

BPE (Bio Processing Equipment) CIP task group

AWS-American Welding Society

D18 Team committee for sanitary welding

3A-Sanitary Standards

Member of board of directors and task committees

In-house engineering and operations

Custom engineered to order – solidworks 3D Cadd designs

Electrical design and programming in-house

Manufacturing work team dedicated to Bio-Pharm

Authorized UL panel shop

ASME certified shop – welding inspector and trainer

Project Management – manage Gantt scheduling, change orders, FAT

Complete Technical Service Staff offering:

Documentation

Field start-up and training

Factory support after start-up



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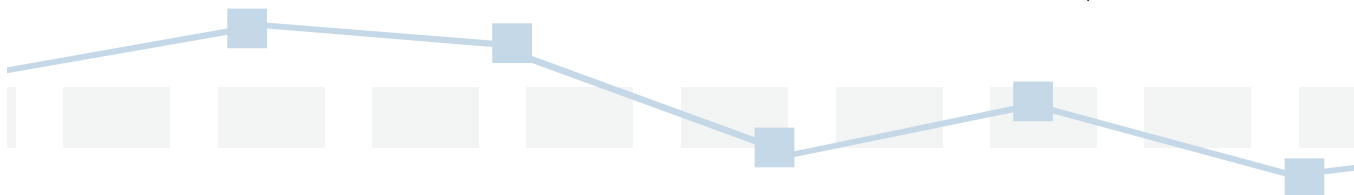
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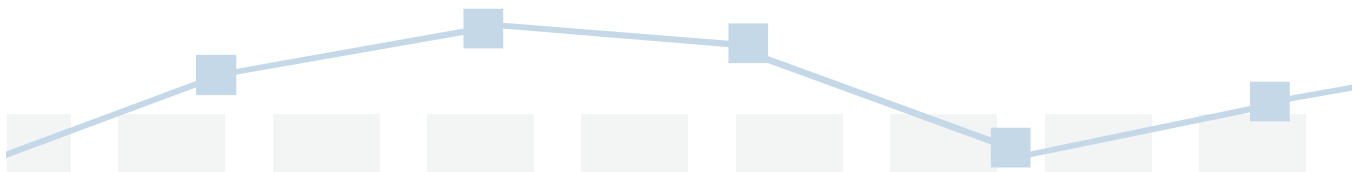
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STARLIMS Corporation delivers cost effective, easy-to-use collaborative LIMS solutions to organizations within the public health, pharmaceutical, forensics, food and environmental industries.

The STARLIMS full featured, flexible, multilingual laboratory information management system provides complete traceability leading to regulatory compliance, without compromising process versatility.

The company's 20-year track record together with STARLIMS' architecture have earned us recognition for "future proofing" our customers' investments in internal know-how and for straightforward conversions of disparate legacy systems.

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