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Monoclonal Antibody Production and Purification

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Abstract
Monoclonal antibody (mAb) therapy is a form of immunotherapy that uses mAbs to bind mono-specifically to certain cells or proteins. This may then stimulate the patient's immune system to attack those cells. MAbs are currently used to treat medical conditions such as cancer, diabetes, arthritis, psoriasis, and Crohn's Disease, but have the potential to treat countless diseases and disorders. In 2015, the mAb market was valued at $85.4 billion, and is expected to reach $138.6 billion by 2024.[1] In manufacturing, mAbs are typically produced in suspension in a series of fed-batch bioreactors using genetically engineered cells originally obtained from Chinese Hamster Ovaries (CHO).[2] In this proposal, two upstream bioreactor designs were analyzed for economic comparison given an annual production goal of 100 kg of mAb, with the first design culminating in a 20,000 L volume at low mAb titer and the second design culminating with a 2,000 L volume at high mAb titer. Following upstream mAb production, the protein was purified to meet clinical FDA standards using a series of downstream purification techniques, including centrifugation, filtration, and chromatography. The two designs can be modeled for both an on-patent and off-patent mAb in order to ensure long-term economic viability. In this project, the drug was modeled based on Ocrevus (ocrelizumab), a humanized therapeutic mAb brought to market in 2017 that targets a CD20-positive B cell to treat the symptoms of both primary progressive and relapsing Multiple Sclerosis.[3] For an off-patent drug, it is recommended that the mAb be priced at $35,000 per 1200 mg annual treatment in order to earn a 15% Internal Rate of Return (IRR) within 5 years of market uptake. For an on-patent drug, a price of $65,000 per 1200 mg treatment should be used to recover the R&D costs of developing a new drug and sunk cost of past unsuccessful drugs. After analyzing both designs, it was concluded that the second, smaller design scheme is more scalable, less risky, and more cost effective for the production of both the on- and off-patent drugs.

Disciplines
Biochemical and Biomolecular Engineering | Chemical Engineering | Engineering

Monoclonal Antibody Production and Purification

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April 17, 2018

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Professor Bruce Vrana
University of Pennsylvania
Department of Chemical and Biomolecular Engineering
220 S. 33rd Street
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Dear Professor Vrana,

Enclosed are detailed process designs and economic analyses comparing two different bioreactor design schemes for monoclonal antibody (mAb) drug substance production. The project proposal specified an annual production goal of 100 kg mAb with a 90% process uptime. The goal of our analysis was to design a process that would meet these requirements and recommend a selling price that would provide a 15% internal rate of return (IRR). To more accurately model this production project, we decided to base our design and economic decisions on a mAb that has recently entered the market, Ocrevus (ocrelizumab). Using these parameters, we evaluated the economic potential of our design schemes using both an on-patent and off-patent framework.

After careful consideration of the variables affecting drug quality and manufacturing requirements, we designed two production schemes. The first upstream scheme culminates in a 20,000 L large production bioreactor, resulting in 25 kg of mAb per batch after downstream purification. The second upstream scheme ends in a 2,000 L small production bioreactor to produce 6.3 kg mAb per batch after downstream purification. Both designs are capable of meeting the 100 kg annual production requirement within four to six months of the year. In order to earn a 15% IRR within 4-6 years of production launch, we recommend pricing the off-patent drug at $35,000 per 1200 mg annual treatment, and the on-patent drug at $65,000 per 1200 mg. Considering both the economic and engineering analyses, we recommend implementing the second, small bioreactor scheme, as it is more flexible, less risky, and more lucrative for the production of both the on- and off-patent drugs.

Sincerely,

Hope McMahon Jessica Schwartz Shritama Ray

Table of Contents

1. Abstract

Monoclonal antibody (mAb) therapy is a form of immunotherapy that uses mAbs to bind mono-specifically to certain cells or proteins. This may then stimulate the patient's immune system to attack those cells. MAbs are currently used to treat medical conditions such as cancer, diabetes, arthritis, psoriasis, and Crohn's Disease, but have the potential to treat countless diseases and disorders. In 2015, the mAb market was valued at $85.4 billion, and is expected to reach $138.6 billion by 2024.[1] In manufacturing, mAbs are typically produced in suspension in a series of fed-batch bioreactors using genetically engineered cells originally obtained from Chinese Hamster Ovaries (CHO).[2] In this proposal, two upstream bioreactor designs were analyzed for economic comparison given an annual production goal of 100 kg of mAb, with the first design culminating in a 20,000 L volume at low mAb titer and the second design culminating with a 2,000 L volume at high mAb titer. Following upstream mAb production, the protein was purified to meet clinical FDA standards using a series of downstream purification techniques, including centrifugation, filtration, and chromatography. The two designs can be modeled for both an on-patent and off-patent mAb in order to ensure long-term economic viability. In this project, the drug was modeled based on Ocrevus (ocrelizumab), a humanized therapeutic mAb brought to market in 2017 that targets a CD20-positive B cell to treat the symptoms of both primary progressive and relapsing Multiple Sclerosis.[3] For an off-patent drug, it is recommended that the mAb be priced at $35,000 per 1200 mg annual treatment in order to earn a 15% Internal Rate of Return (IRR) within 5 years of market uptake. For an on-patent drug, a price of $65,000 per 1200 mg treatment should be used to recover the R&D costs of developing a new drug and sunk cost of past unsuccessful drugs. After analyzing both designs, it was concluded that the second, smaller design scheme is more scalable, less risky, and more cost effective for the production of both the on- and off-patent drugs.

2. Introduction and Objective Time Chart

2.1 Project Background

Monoclonal antibodies (mAbs) are proteins that bind to specific cellular targets and activate the body's immune system for subsequent destruction. MAbs are used in clinical therapy to treat medical conditions such as cancer, diabetes, arthritis, psoriasis, and Crohn's Disease, and have been the focus of the biopharmaceutical industry in recent years. The mAb proteins are derived from a single immune cell and can target a specific cell surface receptor for destruction. The antibody derived from this immune cell can be isolated and engineered to be secreted by a host cell line for clinical treatment. MAbs are often have a high degree of similarity, allowing a given manufacturing scheme to be used for several mAb therapies with minimal alterations to process design.[4] During bioreaction steps, mAbs are secreted by the cells into the liquid growth medium. Following production, the cell suspension undergoes a series of downstream process steps to purify, concentrate, stabilize, and package the mAbs using methods that preserve medicinal efficacy and ensure a virus-free product.[2] An overview of a typical production scheme is shown in Figure 2.1.

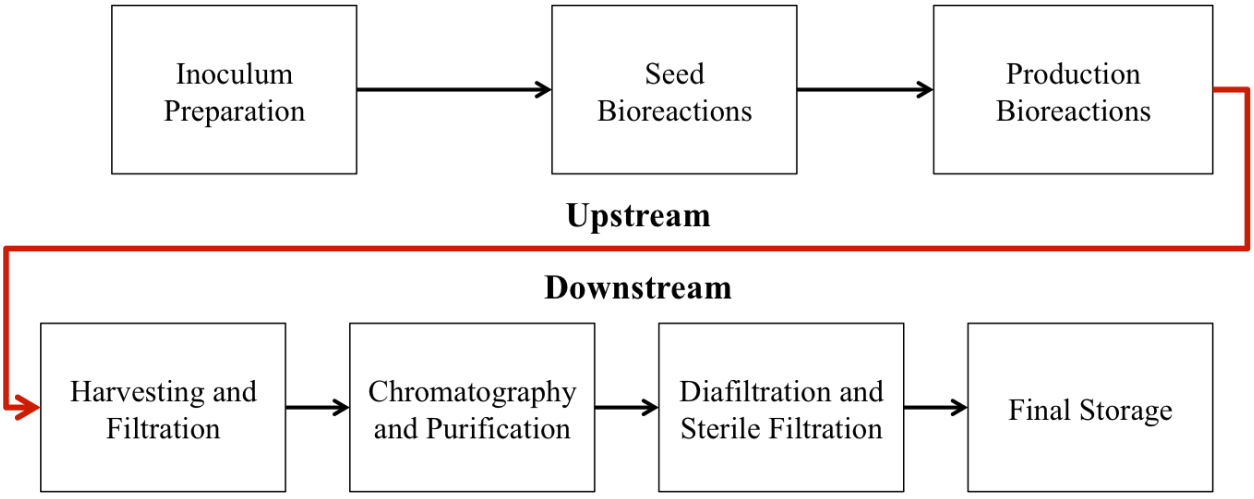


Figure 2.1 A typical mAb production process. The upstream steps grow the cells and express the protein, while the downstream steps isolate and purify the protein product.

At the industrial scale, biopharmaceutical companies such as Genentech produce upwards of 100 kg of a given product every year, and must have the capacity to scale up or down as needed. To model typical production practices at companies with larger operations, this project process has been designed to achieve a 100 kg production goal of a mAb in a four to six month

span. Other recent trends in mAb production, such as the use of single-use disposable bioreactors and the implementation of high-throughput systems, are being implemented to reduce overall capital investment and labor costs.

2.2 Design Schemes

The growing demand for mAb therapies has given rise to the rapid development of high-yielding and robust manufacturing processes. Production bioreactors can be as large as 25,000 L in many traditional scenarios. However, there are several risks and limitations associated with producing such large batch volumes. When scaling up to such large culture volumes, oxygen transfer decreases, aggregation of cells and mAb is more prevalent, and CO_2 stripping becomes difficult to control without exceeding gas sparging flow rate limitations. This results in decreased cell viability, specific mAb productivity by the cells, and product quality.[5] Also, there is a higher risk associated with each batch in the case of malfunction or contamination, in which case the entire batch would be void. To mitigate these outcomes, large upstream batch volumes must produce protein in low titers below 4 g/L. To eliminate these concerns, advances in mammalian cell culture techniques have increased mAb productivity of engineered host cell lines, which allow for higher protein titers well beyond 5 g/L to be produced in smaller batch volumes.[6] For the same reasons outlined above, smaller batch volumes have lower risk, higher cell viability, and higher product quality.

To compare these upstream production scenarios, two upstreams schemes have been designed with corresponding downstream designs. The first scheme is a large production bioreactor process with a low protein titer (2.97 g/L), and the second scheme is a small production bioreactor process with a higher protein titer (6.41 g/L). Both schemes make extensive use of disposable, single-use technologies. The recent industry uptake of single-use equipment has been robust, due to its increased efficiency and cost reduction potential.[7] The design of these schemes is described in more detail in Section 10.

2.3 Ocrevus ™

In order to evaluate this project under real-world constraints, a specific mAb product, Ocrevus, was selected. Ocrevus (ocrelizumab) is a humanized therapeutic mAb that targets a CD20-positive B cell. On March 28, 2017, Ocrevus was approved by the FDA for the treatment of relapsing and primary progressive forms of multiple sclerosis (MS). Ocrevus was discovered, developed, and now marketed by the Roche subsidiary, Genentech.[3]

MS is a chronic neurological disease without a cure, affecting over 400,000 people in the United States. In MS patients, the immune system attacks the insulation around nerve cells in the brain, spinal cord and/or optic nerves, resulting in inflammation and often debilitating symptoms. The majority of people living with MS either have a relapsing form (RMS) or primary progressive multiple sclerosis (PPMS) at the time of diagnosis. RMS is characterized by episodes of new or worsening symptoms, defined as relapses, followed by periods of recovery. PPMS is a highly disabling form of MS characterized by steadily worsening symptoms, usually without periods of improvement or remission.[8]

Ocrevus is the first drug on the market to be approved for the PPMS in addition to RMS. In clinical studies, it was shown to reduce relapses per year by nearly half and reduce disability in RMS patients. It was also shown to be the first treatment to significantly slow disability progression in PPMS patients. Ocrevus is administered intravenously in 600 mg doses every six months. The first dose is a 300 mg intravenous infusion, followed by a second 300 mg infusion two weeks later. Going forward, patients receive 600 mg infusions every 6 months. The price for the first annual treatment of 1200 mg is $65,000. The market performance and attributes of this drug have been used for the design decisions and economic evaluation.

2.4 Objective Time Chart

N/A

2.5 Project Charter

Project Name: Monoclonal Antibody Production, Purification, and Packaging
Project Leaders: Hope McMahon, Shritama Ray, Jessica Schwartz
Specific Goals: Design a process for producing mAbs within an existing biopharmaceutical company to obtain a sales price for an internal rate of return (IRR) of 15% based upon two schemes, one considering only capital investment and the other considering capital investment, research and development (R&D) costs, and risk adjustment.

Project Scope

In Scope:

- Upstream manufacturing process for mAb including growing CHO cells from frozen inoculum of cells to final growth step and mAb production
- Design process to include large production bioreactor (20,000L)
- Design process to include multiple small production bioreactors (2,000L)
- Downstream purification process starting with centrifugation to final sterile filtration and bulk drug substance storage.
- Maintain process integrity and compliance by adhering to good manufacturing practices (GMP)
- Compare both process designs including and excluding R&D costs to generate a sales price per gram to ensure a 15% IRR.
- Determine which process design is optimal by evaluating cost, risk, and product quality

Out of Scope:

- Research and development of monoclonal antibody
- Cell line development
- Packaging and distribution of drugs
- Clinical Trials
- FDA approval of process

Deliverables

Business Opportunity Assessment

- What is the current market for monoclonal antibodies?

Technical Feasibility Assessment

- Is it feasible to produce 100 kg of mAb in 4-6 months using both design scenarios?

Manufacturing Capability Assessment

- What is the capital investment for the manufacturing facility?
- Will the process satisfy the FDA for a pure, consistent product?

Timeline

Facility and process design along with 10 years of production & sales

3. Innovation Map

N/A

4. Market and Competitive Analyses

4.1 Competitive Landscape

The motivation for this project stems from the increasing demand for mAb therapies and the rapidly evolving production platforms. The mAb market was valued at $85.4 billion in 2015 and is expected to reach $138.6 billion by 2024.[1] This growth will be driven by increasing R&D for mAbs and supportive government initiatives, which can be attributed to growing demands for personalized medicine in addition to specific benefits associated with mAb therapy such as fewer adverse effects, homogeneity, specificity, and large-scale production.

Additionally, the MS treatment market was valued at an estimated $17.2 billion in 2015 and is expected to grow at a 1.5% compound-annual growth rate (CAGR) to reach $20 billion by 2024.[9] Since Ocrevus is the first drug approved to treat multiple forms of MS, it is expected to be a blockbuster drug and the specialist community is certain that it will assume a dominant position in the MS market over the next 3 to 5 years. The drug has shown high efficacy in both forms of the disease, has a reasonable safety profile, and has a price tag of $65,000 per 1200 mg treatment, which is a 20% discount from the average list prices of its competitors.[10]

Other MS treatments on the market include Biogen's Tysabri and Tecfidera, Novartis' Gilenya, and Teva's Copaxone. Copaxone was previously a market leader, being the first non-interferon to enter the market, while Tecfidera had the fastest market uptake in the field. Analysts expect 40%-50% erosion of Tysabri, and 30%-40% erosion of Tecfidera and Gilenya sales once Ocrevus is taken up by the market. Ocrevus is also anticipated to surpass historical performances due to its novel indication of use, high efficacy, convenient dosing, reasonable safety, and modest pricing.[10]

4.2 Sales Forecast

Since its approval in March 2017, Ocrevus saw 12-month sales of $1.4 billion from Q2 2017 to Q1 2018.[11] At $65,000 per treatment, it is estimated that 20,000 treatments were administered. The revenues are projected to grow rapidly and soon dominate the MS market. These metrics and predictions have been used to create sales forecasts in order to evaluate the economic viability of the two designs presented in this project.

In order to build the forecast, 10-year sales for an Ocrevus competitor, Gilenya, were extracted from Novartis' annual reports.[12] The annual year-over-year (YOY) growth rates were calculated to build a model representative of the anticipated market uptake for an MS mAb drug. This

growth model was then applied to the known Year 1 Ocrevus sales to build an 8-year forecast, which is depicted in Table 4.1. The growth is rapid in the first few years during initial market uptake, but slows significantly after Year 4. This trend is illustrated in Figure 4.1. These forecasts are indicators of market demand and were used to design the annual production schedule. They also dictate the forecasted annual revenue, which is built into the profitability analysis in Section 21.

Table 4.1. Sales Forecast Construction of Ocrevus. Gilenya YOY growth rates were applied to Year 1 sales of Ocrevus to build a representative 8-year sales model.

YEAR	Gilenya Sales ($MM)	YOY % Growth	Forecasted Ocrevus Sales ($MM)
1	494	N/A	1,377
2	1,195	142%	3,331
3	1,934	62%	5,397
4	2,477	28%	6,908
5	2,776	12%	7,737
6	3,109	12%	8,666
7	3,185	2%	8,839
8	N/A	2%	9,016

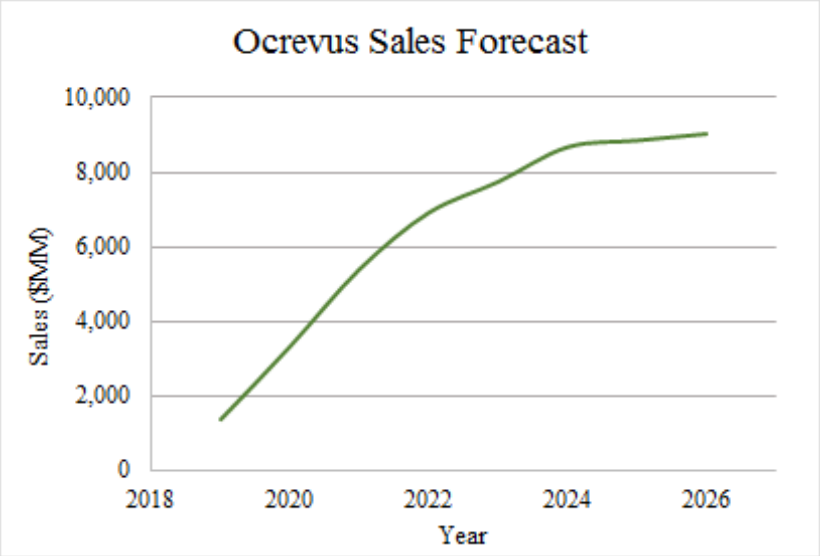


Figure 4.1. Projected Ocrevus sales based on historical Gilenya sales data. The growth rate is plateaus around 2022 (Year 4).

5. Customer Requirements

N/A

6. Critical-to-Quality Variables

Because therapeutic protein products impact human life, quality is an essential consideration in the highly regulated biopharmaceutical industry. The U.S. Food & Drug Administration (FDA) dictates and enforces Quality by Design (QbD), a systematic approach to development based on quality and risk-management. It begins with predefined objectives and emphasizes science-driven product and process understanding and control.[13] This involves defining the Quality Target Product Profile (QTPP), a summary of the quality characteristics of the drug product that will ideally be achieved to ensure the desired quality while accounting for safety and efficacy. QTPP elements include dosage form & design, route of administration, dosage strength, pharmacokinetics, stability, and drug product quality attributes.

Ocrevus is administered by intravenous (IV) infusion, and is supplied in single dose 15 mL vials containing 300 mg of ocrelizumab at a nominal fill volume of 10.0 mL. The final formulation includes sodium acetate, trehalose dihydrate, and 0.02% (w/v) polysorbate 20, pH 5.3. Prior to administration, it is diluted with 0.09% sodium chloride solution to reach a protein concentration of approximately 1.2 mg/mL.[14]

As the scope of this project excludes drug product filling and packaging processes, the quality standards for the bulk drug substance are most relevant. The Critical Quality Attributes (CQA's) of the Drug Substance are shown in Table 6.1. These attributes and requirements have guided the design of the operating parameters, equipment selection, and control strategy.

Table 6.1 Critical to Quality Attributes of the Drug Substance

CQA	Risk	Origin
Host Cell Protein (HCP)	Safety & immunogenicity	Process-related impurities
Host Cell DNA	Safety	Process-related impurities
Adventitious Viral Agents	Safety	Likely introduce during cell-culture operations
Bioburden	Safety, Purity, and Efficacy; Degradation or modification of product by contaminating microorganisms	Bioburden can be introduced by raw materials and throughout the manufacturing process
Endotoxins	Safety and Purity	Endotoxins can be introduced by raw materials and throughout the manufacturing process
Mycoplasma	Safety	
Appearance (color, clarity, and opalescence)	Safety and Efficacy	N/A
Leachables/extractables	Safety	Leachables and extractables could be introduced by any product contact equipment, containers, and consumables
Osmolality	Safety	Osmolality is impacted by formulation. No change is expected during storage.
Polysorbate 20	Safety	Polysorbate 20 is added during DS formulation.

7. Product Concepts

N/A

8. Superior Product Concepts

N/A

9. Competitive Patent Analysis

Many pharmaceutical companies file patents on their drug discoveries to claim rights to a formulation and ensure exclusivity in the marketplace. Currently, the term of a new patent is 20 years from the date on which the application for the patent was filed in the U.S. During the 20 year patent term, this company claims the sole rights to manufacture and distribute the drug.[15] Roche's patent on Ocrevus was filed on September 24, 2007, and will thus expire in 2027. For the duration of the patent, only Roche is allowed to legally manufacture, sell, and administer Ocrevus.

Once a patent term expires, other competitors are able to enter the market and administer the formulation as a generic, off-patent product. When this happens, the price of the drug almost always drops in order for companies to stay competitive. The typical price drop for a physician-administered biopharmaceutical product is 38 - 48%.[16] For example, when Ocrevus goes off-patent in 2027, it can be expected that the price of a 1200 mg treatment will drop from $65,000 to between $33,800 and $40,300.

This pricing difference plays a key role in evaluating the economic viability of a drug manufacturing project. For this reason, two economic frameworks have been considered in this design. The first is an off-patent framework, in which only capital investment and annual operating costs will be considered in the profitability analysis. The second framework is designed for an on-patent drug, which will require all R&D expenditures, clinical trial operations, and drug success probabilities to be factored into the evaluation in addition to the capital investment and annual operating costs. Further details for these two evaluations are presented in Section 21.

10. Preliminary Process Synthesis

The overall process flow of mAb production and processing is standardized across the industry.[2] Figure 2.1 illustrates a general block flow diagram for this process, with each step representing opportunities for design decisions.The overall process is split into three upstream sections and three downstream sections. Because the upstream bioreaction and downstream purification steps are largely independent, design considerations for upstream and downstream steps were evaluated separately. Design decisions were made to determine the number, type, and capacity of seed and production bioreactors, the production capacity of the downstream process, and the types of chromatography used in later downstream purification steps. Since the downstream process uses smaller equipment in series, it can be scaled for several possible upstream combinations.

When designing the upstream processes, the amount of mAb produced for the same liquid volume can be increased without significantly raising costs because the equipment and raw materials required for operation will not change. On the other hand, if the amount of mAb produced is kept constant, the cost of a given upstream design will scale with volume because the volume of media and bioreactor largely affect the cost. However, downstream unit capacity always scales with the amount of mAb product per batch, since its cost is based on product-specific separation processes. Therefore, as product titer increases, the cost becomes increasingly dependent on downstream processes as compared to upstream processes.[2]

Two designs were created for this project to compare a large volume, low titer and a small volume, high titer production scenario. The first design scheme, referred to as the Large Production Bioreactor Design, is illustrated in Figure 10.1. It illustrates a more traditional upstream process, in which the bioreaction steps culminate in a 20,000 L, stainless steel bioreactor. Selection of smaller volume bioreactors in inoculum preparation and cell seeding bioreactions was based on cell growth kinetics and production formation requirements as discussed in Section 11.2. The resulting product titer of this upstream design was 2.97 g/L, which is a typical low titer in mAb manufacturing processes.

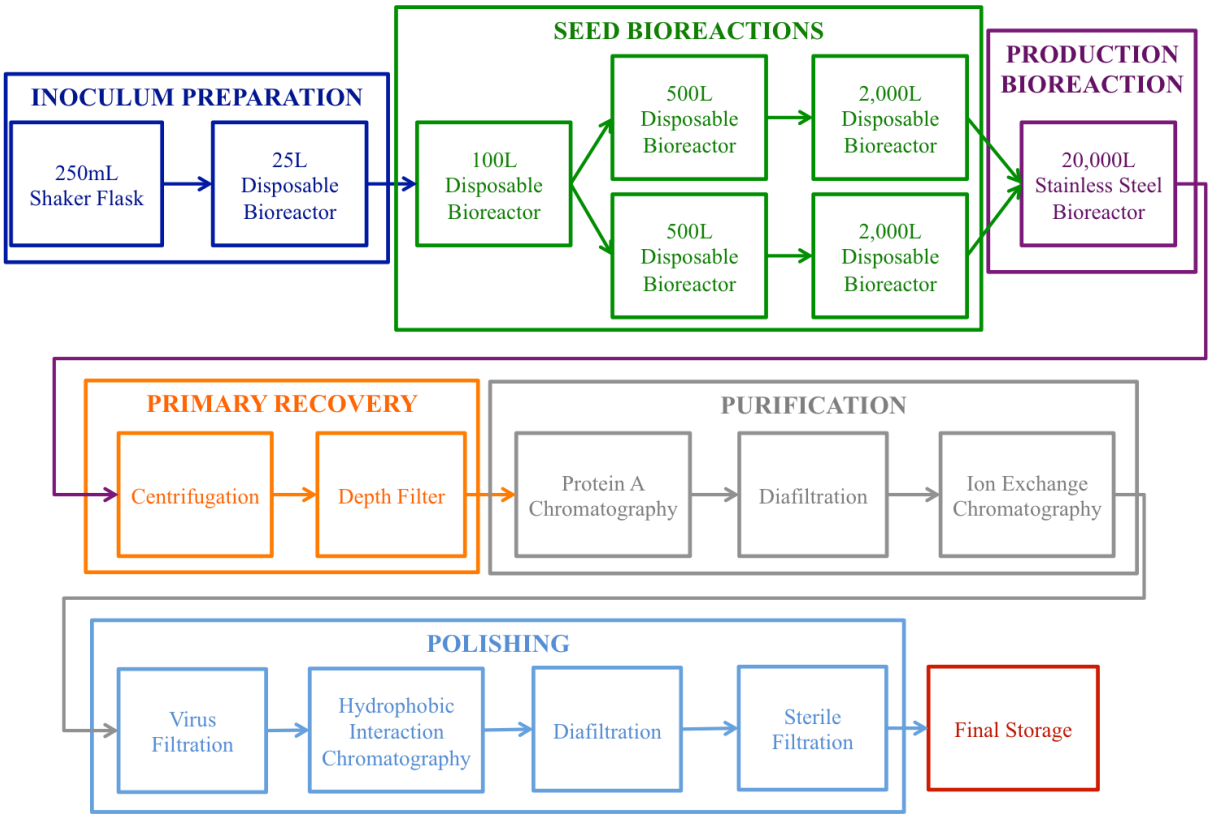


Figure 10.1 Overall block flow diagram of the Large Production Bioreactor Design for mAb production and purification. This design represents a low volume, high titer manufacturing scenario.

The second design scheme, referred to as the Small Production Bioreactor Design, represents a more modern upstream process, incorporating a production bioreactor that has a smaller volume capacity, but handles higher product titers with greater ease. The bioreaction steps in this scheme culminate in a 2,000 L single-use bioreactor, with a product titer of 6.41 g/L, which is approximately double that of the Large Production Bioreactor Design. Due to the smaller final upstream volume, less inoculum preparation and cell seeding steps were required.

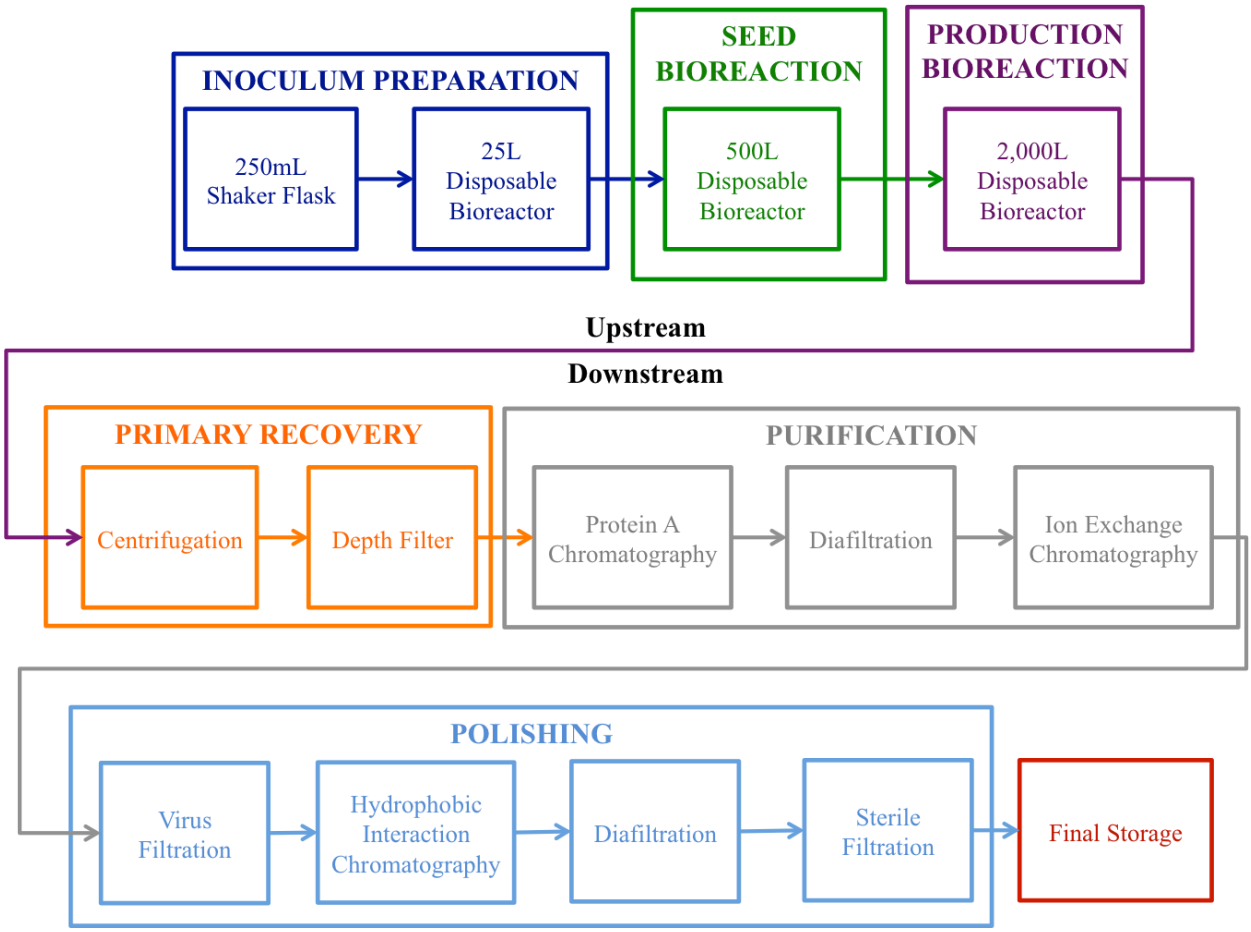


Figure 10.2 Overall block flow diagram of the Small Production Bioreactor Design for mAb production and purification. This design represents a high volume, low titer manufacturing scenario.

For both schemes, the downstream purification process was scaled to match the amount of product produced at the end of the upstream process. Based on this mass, the number of chromatography cycles needed per batch was calculated. Since mAb product is lost in separation and purification steps, an overall yield of 63% was calculated for the downstream process. The upstream processes for both schemes were then adjusted to meet the specified annual production goal of 100 kg of mAb.

11. Assembly of Database

11.1 Chemical Components and Thermophysical properties

Water was used as the main reference component for all thermophysical calculations of the mAb product and growth media. Air was also used in bioreaction steps. Other components present were considered negligible in a thermophysical context. Properties of water and air are listed in Table 11.1

Table 11.1 Properties of relevant chemical components in mAb production and purification processes

Chemical Component	Molecular Weight (g/mol)	Heat Capacity (J/g°C)	Density 36.5°C, 1 atm (kg/m^3)	Viscosity (kg/m s)	Cost ($/kg)
Water (WFI)	18.02	4.184	1000	$4.8x10^{-9}$	0.0047
Air	28.96	1.006	1.14	--	--

11.2 Cell Growth Kinetics and mAb Production Rate

Cell growth and mAb production occur in two phases. First, the cells must be grown to a specified peak viable cell density of $9x10^6$ cells/mL, with at least 90% cell viability, as stated by the project charter. Then, the cells reach a growth plateau and product formation occurs linearly given a specific productivity of $3.3x10^{-10}$ g mAb per viable cell. From Equation 1 below, the final density of cells in a given bioreactor can be calculated based on the growth rate and growth time spent in the vessel. In the final process design and scheduling, one day was added to the specified growth time to account for the lag phase of the cells upon initial re-seeding. During the lag phase, the cells are adjusting to their new environment and adhering to the cell surface before entering the exponential log growth phase.

$$ln\left(\frac{N_2}{N_1}\right) = \mu(\Delta t) \qquad (1)$$

where, N_1 = initial cell density (cells/mL)
N_2= final cell density (cells/mL)
μ = growth rate (day^{-1})
Δt = duration of cell growth (day)

In the inoculum preparation steps of the upstream process, which occur within the first 7 days of the overall process, an average growth rate of 0.63 day^{-1} was used. This value was obtained in a feed study utilizing the same CHO DG44 cell line and ActiPro, 7a, 7b feeding regime as will be used in this process.[17] When cells are initially thawed from their cryogenic

state, it can require a few passages, or cell division cycles, to reach full potency. For the remaining duration of the upstream process, the growth rate was calculated from the project-specified peak doubling time of 20 hours. From Equation 2 below, the growth rate was found to be 0.83 day^{-1}.

$$t_D = \frac{ln(2)}{\mu} \quad (2)$$

In order to maintain cell viability higher than 90%, which is a requirement for adequate product formation and quality for the given CHO DG44 cell line, cell dilution and scale-up factor are critical parameters to consider. In culture, cells cannot be diluted by more than a factor of 4 or scaled by more than a factor of 10. If the cells are too dilute in the culture media, the cells will swell and will not take up the required nutrients for growth in order to maintain the osmotic pressure across the membrane and prevent bursting. If the cells are scaled up by more than a factor of 10, the number of cells dying as result of the natural cell cycle will become toxic to cell growth. In addition, the cells will become too crowded and begin to aggregate, which inhibits cell growth and promotes accelerated cell death. As a result, upstream design decisions were made to dilute cells by less than or equal to 4 and scale them up by less than or equal to 10 in equivalent volumes. Both bioreactor volumes and fed-batch strategies were based on these parameters.[43] For culture volumes that are 250L or greater, the bioreactors are only filled to half of the intended final volume initially. The remaining half of the final bioreactor culture volume is fed to the cells in a daily bolus of culture media and feed supplements. These feed supplements provide additional nutrients and can be scaled based on manual daily samples to maintain optimal glucose and amino acid levels. This fed-batch feeding strategy increases the culture volume incrementally, prevents the cells from being too dilute while allowing scale up of factors greater than 10, especially in larger cell seeding steps and in the product formation step.[2, 6]

12. Process Flow Diagram and Material Balances

The process flow diagrams (PFD) and mass balances listed below visualize and characterize the two main process designs. The upstream and downstream PFD's are illustrated separately for both the Large and Small Production Bioreactor Designs. The two downstream processes have the same design, but were scaled for the appropriate volumes. Media preparation schemes are depicted below each of the upstream flowsheets.

12.1 Upstream Process for Large Production Bioreactor Design

The flowsheet in Figure 12.1 portrays the upstream portion of the Large Production Bioreactor design, which concludes in a 20,000 L stainless steel production bioreactor. The solution of media, cells, and mAb in this production bioreactor are then passed onto to the primary recovery step of downstream purification. Streams labeled "Media Prep" refer to the media preparation schemes illustrated in Section 12.1.1. The flowsheet for the corresponding downstream purification process are illustrated in Section 12.2.

12.1.1 Upstream PFD for Large Production Bioreactor Design (PFD 01)

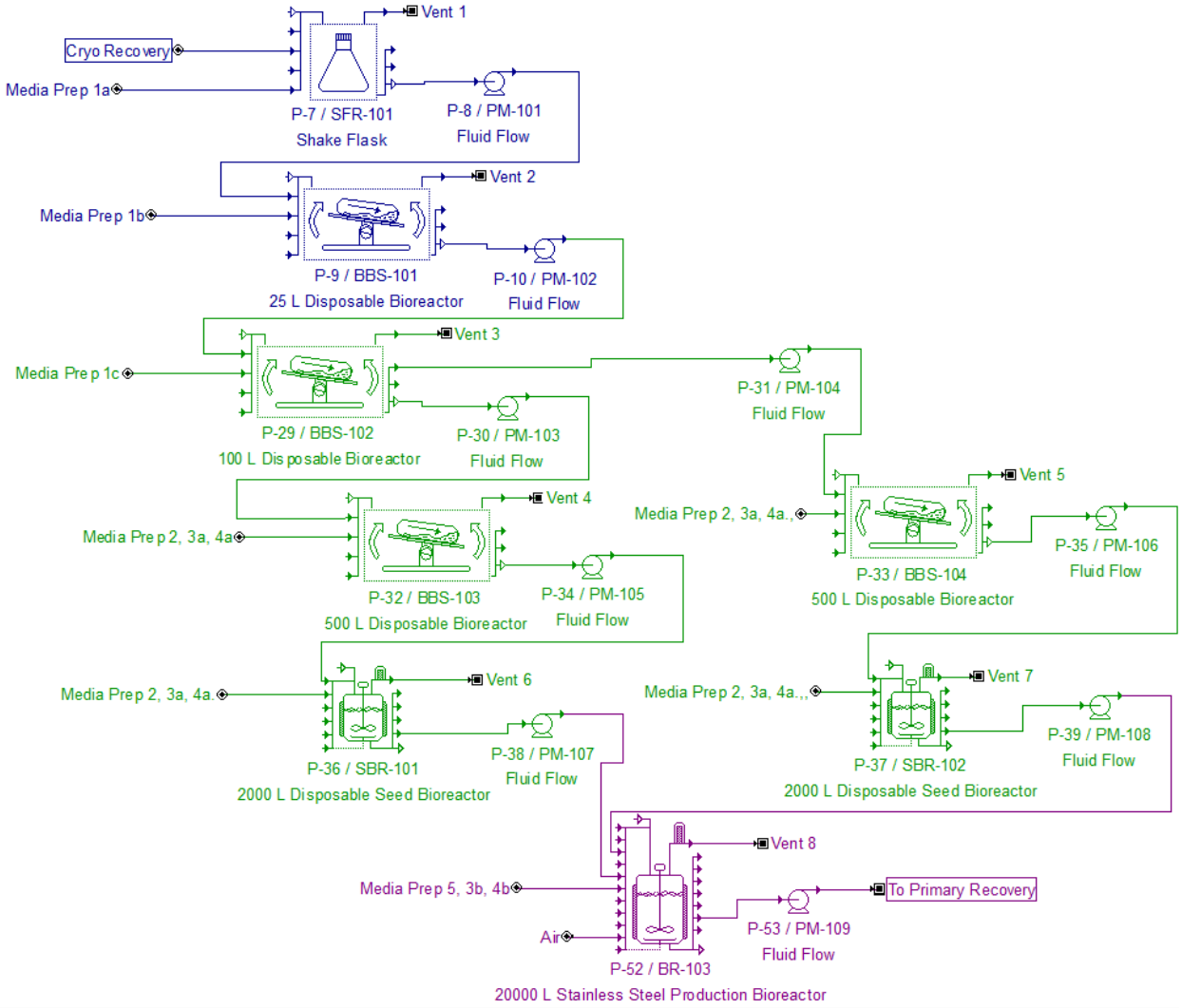


Figure 12.1 Upstream PFD for mAb production for the Large Production Bioreactor Design.

12.1.2 Media Preparation Scheme for PFD 01

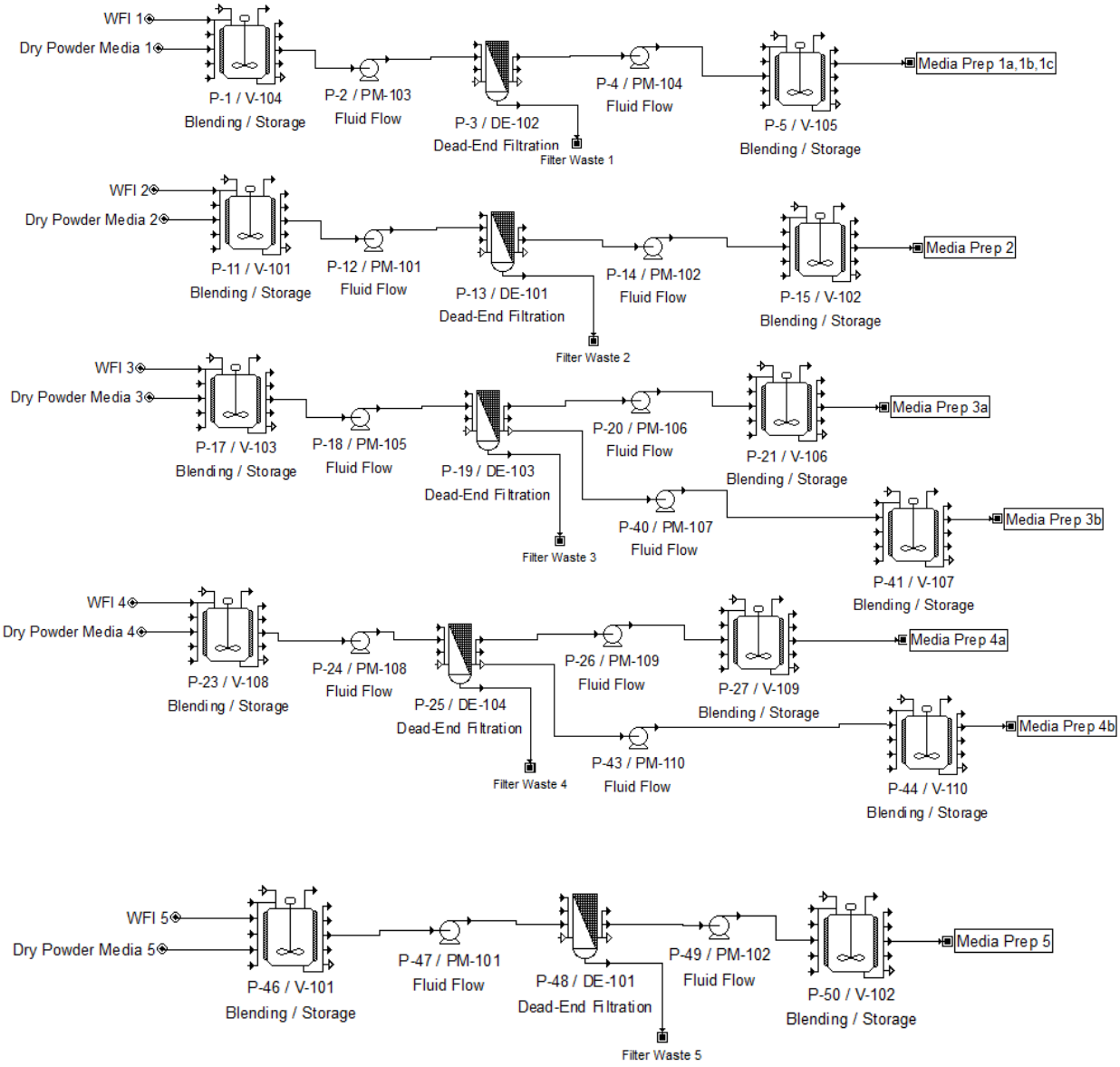


Figure 12.2 A detailed flow diagram of "Media Prep" streams in PFD 01 for mAb production in the Large Production Bioreactor scheme.

12.1.3 Overall Mass Balance for PFD 01

Components (Name)	IN (kg/batch)	OUT (kg/batch)
Cells	0.0000047	75.4
mAB Product	0	40.1
Water (H_2O)	0.03	13500
Glucose ($C_6H_{12}O_6$)	721	0
Glutamine ($C_5H_{10}O_3N_2$)	70	0
Oxygen	2983	0
Carbon Dioxide (CO_2)	0	463
Ammonia (NH_3)	0	7.4
Lactate ($C_3H_6O_3$)	0	136.6
TOTAL	3493	14223

12.2 Downstream Process for Large Production Bioreactor Design

12.2.1 Downstream PFD for Large Production Bioreactor Design

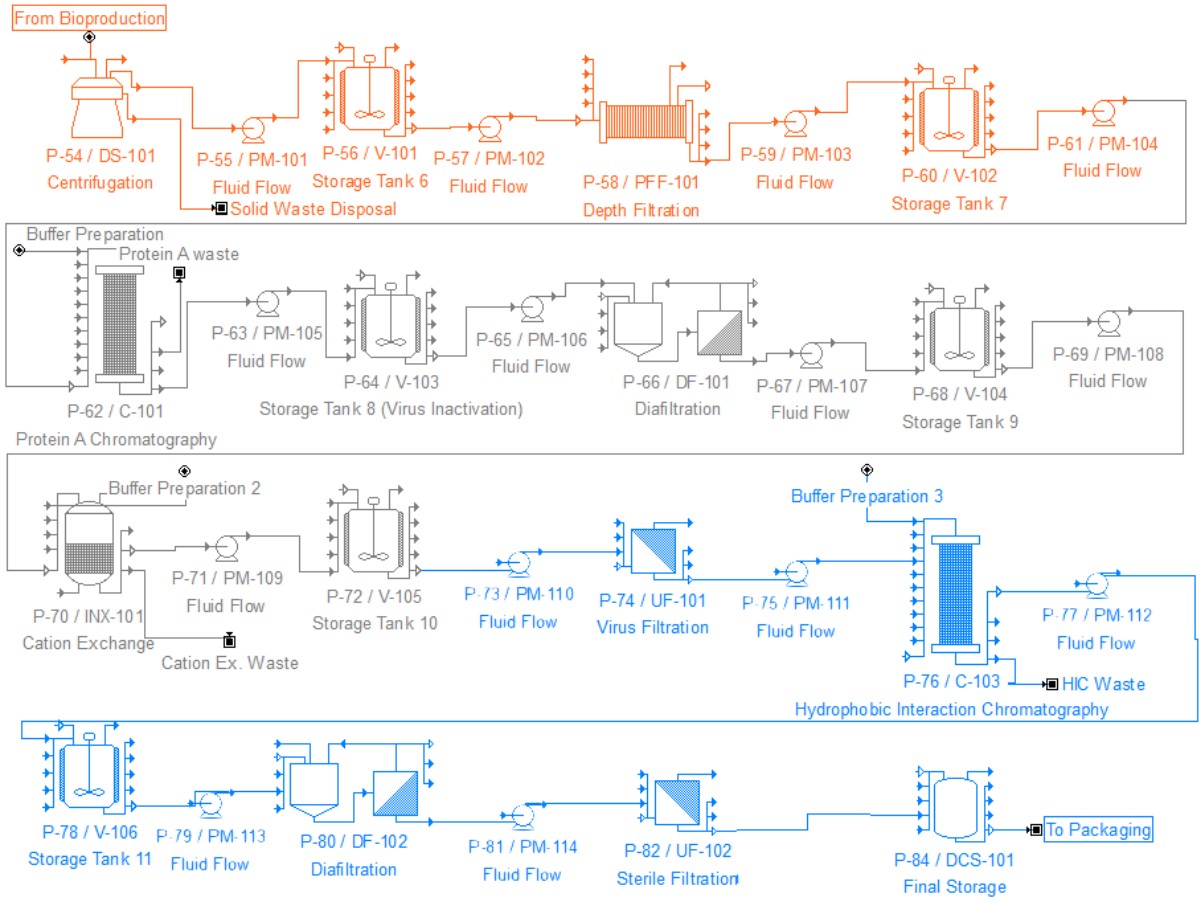


Figure 12.3 Downstream PFD for for mAb purification in the large production bioreactor design. The downstream will be run 1 time per batch.

12.2.2 Overall Mass Balance for PFD 02

Components (Name)	IN (kg/batch)	OUT (kg/batch)
Cells	75.4	0
Water (H_2O)	13500	700
mAb Product	40.1	25.2

12.3 Upstream Process for Small Production Bioreactor Design (PFD 03)

The flowsheet in Figure 12.3 portrays the upstream portion of the Small Production Bioreactor design, which concludes in a 2,000L stainless steel production bioreactor. The solution of media, cells, and mAb in this production bioreactor are then passed onto to the primary recovery step of downstream purification. Streams labeled "Media Prep" refer to the media preparation schemes illustrated in Section 12.3.1. The flowsheet for the corresponding downstream purification process are illustrated in Section 12.4.

12.3.1 Upstream PFD for Small Production Bioreactor Design

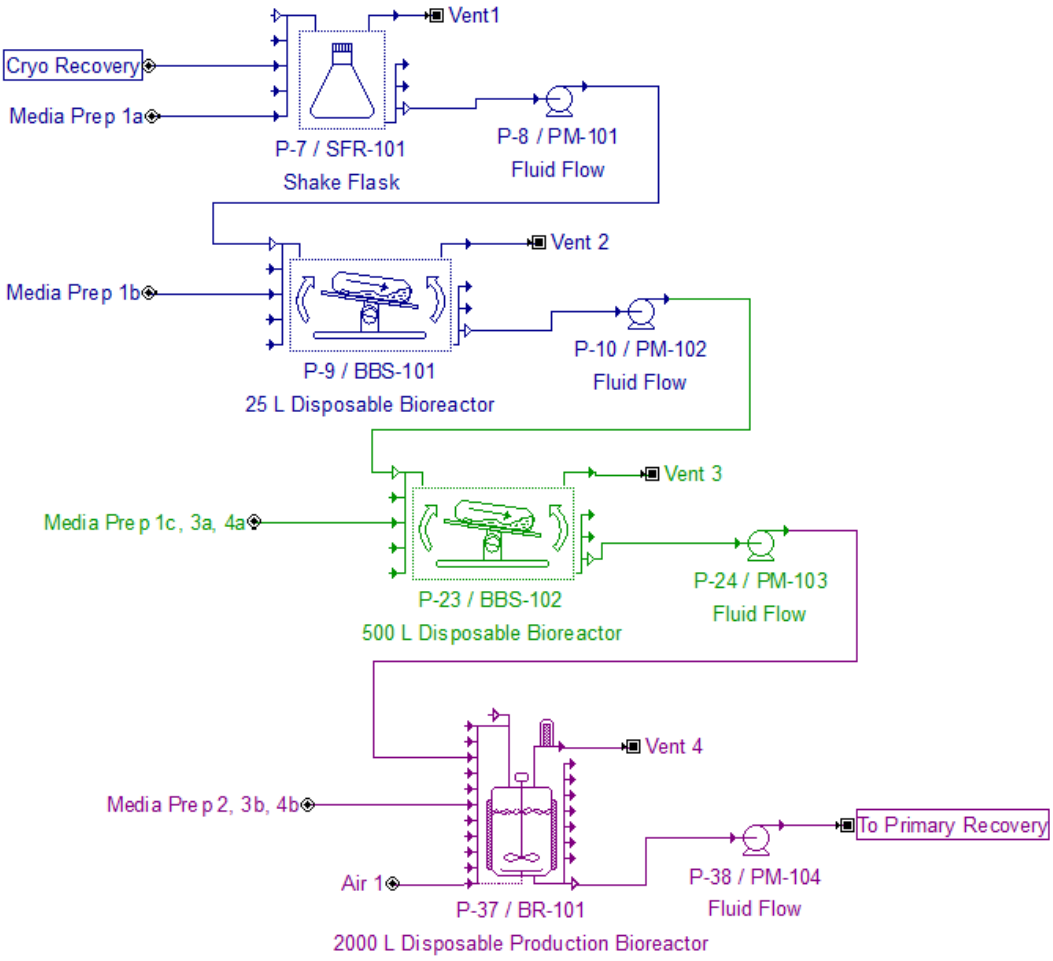


Figure 12.4 Upstream PFD for mAb production in the Small Production Bioreactor scheme. The upstream will be run 1 time per batch.

12.3.2 Media Preparation Scheme for PFD 03

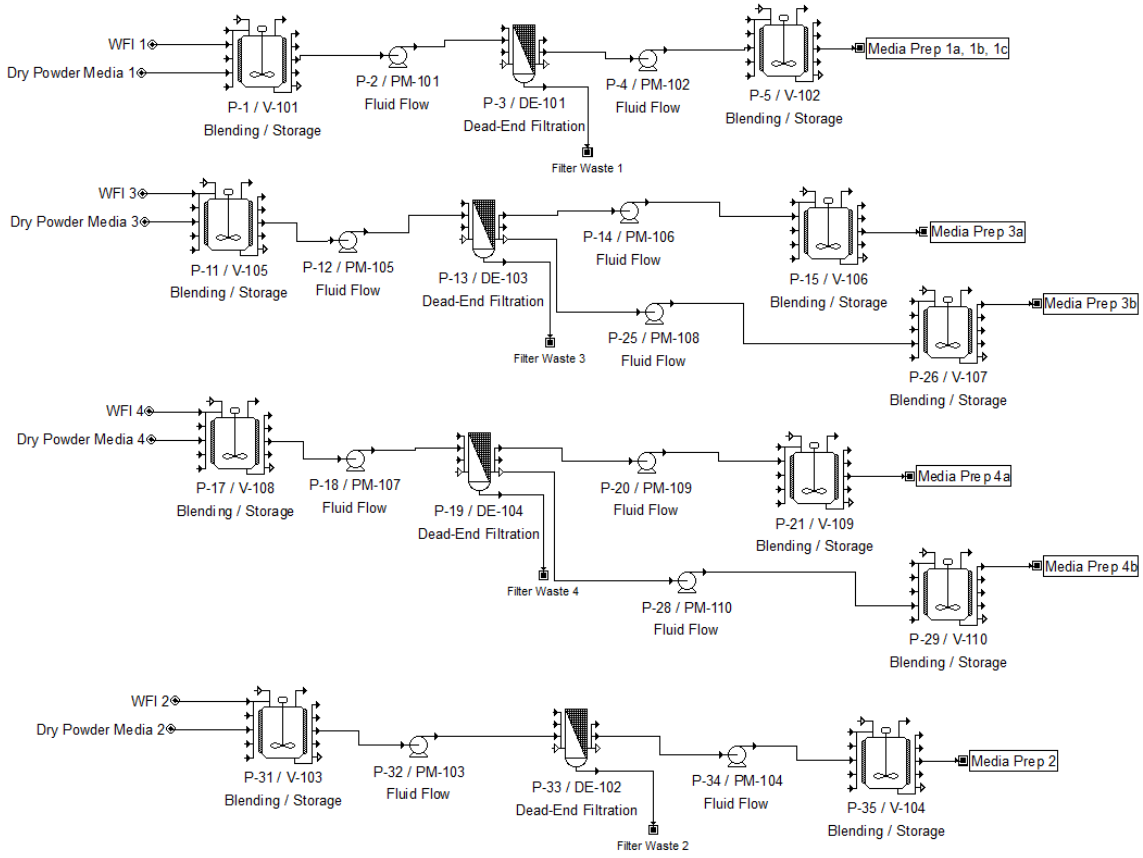


Figure 12.5 A detailed flow diagram of "Media Prep" streams in PFD 03 for mAb production in the Small Production Bioreactor scheme.

12.3.3 Overall Mass Balance for PFD 03

Components (Name)	IN (kg/batch)	OUT (kg/batch)
Cells	0.0000047	29.4
mAB Product	0	40.1
Water (H_2O)	0.03	13500
Glucose ($C_6H_{12}O_6$)	333	0
Glutamine ($C_5H_{10}O_3N_2$)	32	0
Oxygen	2465	0
Carbon Dioxide (CO_2)	0	214
Ammonia (NH_3)	0	3.4
Lactate ($C_3H_6O_3$)	0	63
TOTAL	2830	6590

12.4 Downstream Process for Small Production Bioreactor (PFD 04)

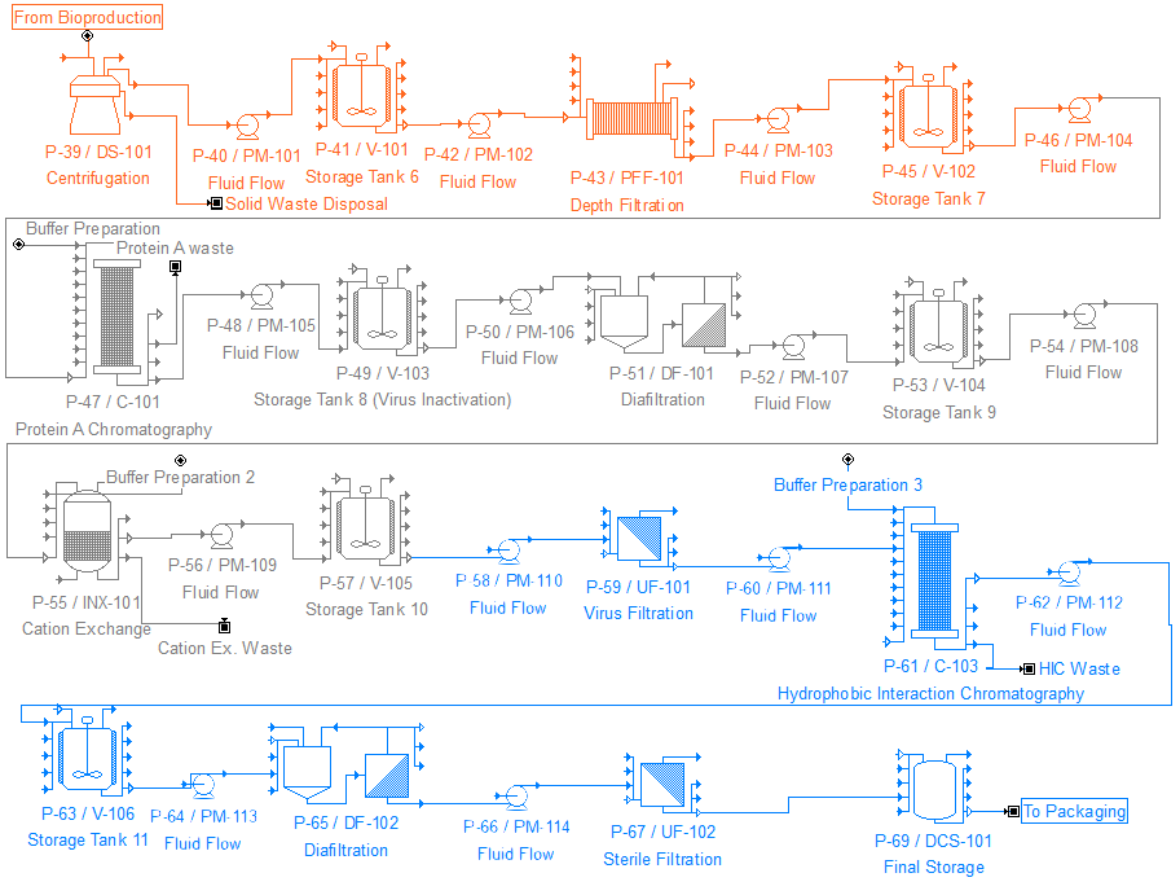


Figure 12.6 Downstream PFD for for mAb purification in the small production bioreactor design. The design is the same as PFD 02, but the units are scaled appropriately. The downstream will be run 4 times per batch, with one cycle being run for each upstream 2,000L production bioreactor.

12.4.2 Overall Mass Balance for PFD 04

Components (Name)	IN (kg/batch)	OUT (kg/batch)
Cells	29.4	0
Water (H_2O)	1560	420
mAb Product	10.0	6.30

13. Process Description

MAb production and purification is divided into upstream and downstream processes. The upstream process objective is to grow the CHO cells up to peak viable cell density such that they secrete mAb into the surrounding growth media. Then, the downstream processes harvest the product from the cell culture solution and purify the remaining protein according to FDA quality standards for commercial use.

13.1 Upstream Production Process Description

In the upstream production of mAbs, there are two phases of growth: cell growth and mAb formation. The inoculum preparation and seed bioreaction steps achieve the first cell growth step, while the final production bioreaction step achieves the second step of mAb formation. The engineered CHO cell line selected for this process was CHO DG44, which was analyzed for nutrient requirements, initial average growth rate, and media formulations in a previous study that was discussed in Section 11.2 [17]. Section 11.2 also outlines how cell density and culture durations were calculated for all upstream processes. Proper preparation of cell culture media formulations in addition to precise control of operational parameters are detailed in the following sections as they are vital for optimal cell growth and product formation. Execution of inoculum preparation, seed bioreaction, and production bioreaction steps are then described for the Large and Small Production Bioreactor Processes. These steps are shown in the process flow diagrams in Sections 12.1 and 12.3.

13.1.1 Media Preparation - Large & Small Production Bioreactor Designs

For both processes, pre-formulated HyClone™ ActiPro™ cell culture medium from GE Healthcare Life Sciences will be used. The media has been designed for high-yield recombinant protein production via CHO cells in a batch or fed-batch process, and is chemically defined and animal-derived-component-free. This provides consistency across batches as there are known concentrations of all chemical components and no complex contaminants.

13.1.1.1 Growth Media

For all inoculum steps and bioreactor, dry powder growth medium medium will be mixed with water-for-injection (WFI) at 25°C. The complete protocol for reconstituting dry powder ActiPro™ medium can be found in Appendix B. The final pH of the mixture should be in the neutral range with

osmolality ranging 270 to 330 mOsmol/kg. The prepared growth media will then flow perpendicularly through a sterile 0.2 μm, hydrophilic polyethersulfone (PES) membrane filter with a filtration area of 0.57 m^2 to remove large contaminants. This is followed by transfer to a storage tank for storage at 4°C until further use. Transfer steps will occur via peristaltic pump at flow rates corresponding to the volume of media being prepared.

13.1.1.2 Feed Supplement Media

Feed supplements HyClone™ CellBoost™ 7a and CellBoost™ 7b will be used in production steps for both processes, which are also chemically defined and animal-derived-component-free for recombinant protein production. The feeds are concentrated nutrients that are complementary used in conjunction to maintain nutrient concentrations at appropriate values for growth. CellBoost 7a contains amino acids, vitamins, salts, glucose, and other trace elements. CellBoost 7b contains concentrated amino acids. For preparation, each dry powder medium will be mixed with water-for-injection (WFI) at 25°C. The complete protocol for reconstituting the dry powder CellBoost™ media can also be found in Appendix B. The mixed CellBoost 7a should have a neutral pH, while the CellBoost 7b should have a basic pH. The prepared medias will each be filtered by a sterile 0.2 μm, hydrophilic polyethersulfone (PES) membrane to remove large contaminants followed by transfer to respective storage tanks for storage at 4°C until further use. Transfer steps will occur via peristaltic pump at flow rates corresponding to the volume of media being prepared.

13.1.2 Operation Set Points and Controls

Both cell culture and mAb production are very sensitive processes that require careful monitoring of conditions and tight control. Main conditions of interest are temperature, dissolved oxygen (dO_2), dissolved carbon dioxide (dCO_2), pH, and osmolality, which are all closely linked to metabolite levels, cell growth, cell viability, cell productivity, and product quality. The relationships between various controlled variables and cell and product variables is illustrated in Figure 13.1.[18] Offline measurements will be performed for cell counting and cell viability, pH verification, osmolality, and metabolite concentrations. Cell counting and viability will be measured

using a hemocytometer assay, while metabolites will be monitored by taking samples from the cell culture. Metabolites of interest are: glucose, glutamine, glutamate, lactate, and ammonia. Glucose, glutamine, and glutamate are consumed by the cells while lactate and ammonia are produced by the cells. However, the cells can also use lactate as a source of potential energy over glucose. Osmolality levels of the culture medium should remain in the range of 270-330 mOsm/kg set during media preparation. Osmolality is measured daily using freezing-point depression osmometry, a technique based on the property that the freezing point of a known solvent decreases when solute is added. The

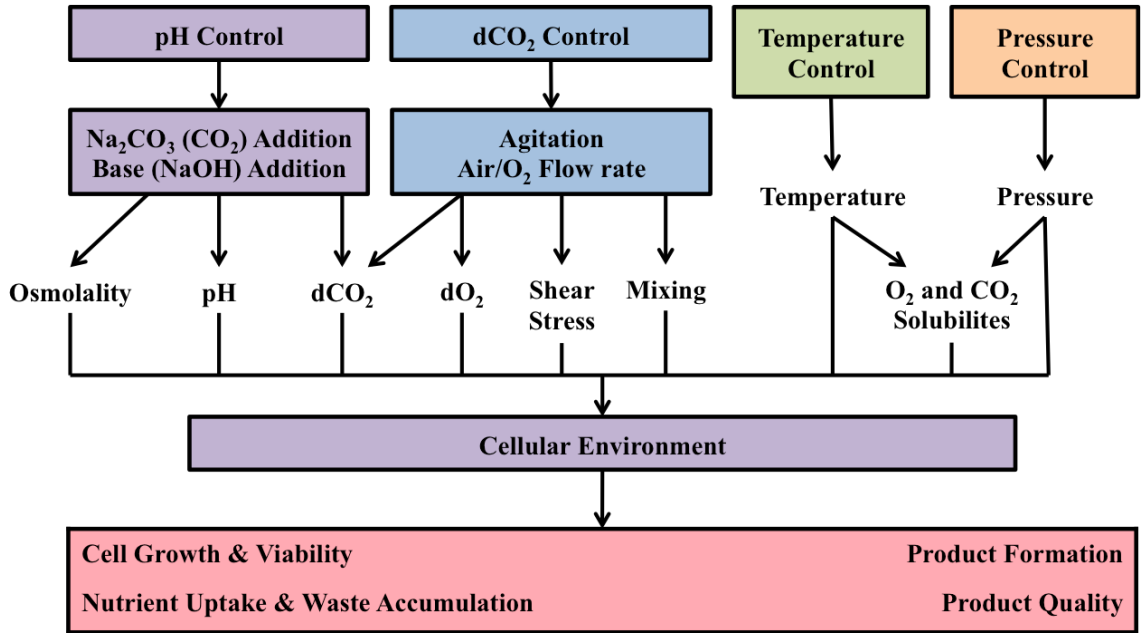


Figure 13.1. Relationship between upstream operation parameters and their effect on both CHO cells and the secreted mAb product.

freezing point is directly related to the number of solute particles present, therefore concentration can be measured with this method. It is preferred to keep osmolality values on the lower end of the acceptable range. In higher cell densities, high osmolality and high dCO_2 levels can lead to growth inhibition and decreased cell productivity relating to mAb formation.

Real-time measurements of temperature, dO_2, dCO_2, and pH will also be performed. For the disposable bioreactors and cell incubator, temperature measurement and control is automated and comes with the devices. The temperature of the 20,000L stainless steel bioreactor in the Large Production Bioreactor scheme will be measured with a temperature probe connected to the heating and cooling jacket of the bioreactor for

control. An acceptable temperature range is between 36 and 37°C, with the ideal setpoint being at 36.5°C.

Another parameter in the disposable bioreactors that has built in probes and controls is dO_2. The setpoint for dO_2 in these processes is 40% of air saturation, however an acceptable range is 20-50%. It is important to prevent low dO_2 levels, as this will lead to excessive lactate synthesis by the cells and lower product yields. Similarly if the dO_2 is too high, the cells will become toxic and likely die. In the 20,000L stainless steel production bioreactor, a Clark type electrode will measure dO_2. To increase dO_2, the agitation and air sparging rate should be increased. For rocking disposable bioreactors, the rocking speed should be increased along with an increase in air sparging. However, it is important that agitation and air sparging rates do not become too high. If rocking or impelled speeds are too high this could result in damaging levels of shear stress on the cells and could lead to excessive bubble formation and foaming. When bubbles are introduced in the culture, they rise to the top and burst, releasing high and harmful energy on the cells below. If these methods do not appropriately correct dO_2 levels, then pure O_2 will be sparged in separately instead of adding more air and creating too many big bubbles. Anti-foaming agent like a pluronic can also be added to reduce foaming and bubbles.

In addition, dCO_2 levels are also extremely important, because CO_2 can inhibit cell growth and product quality. If the dCO_2 is too high, cell growth will be inhibited as CO_2 displaces O_2 in culture and results in an O_2 limiting situation. If it is too low, the solution will become too basic and affect both glucose consumption and lactate production of the cells. Further, CO_2 has a profound effect on the pH of the culture medium as increasing dCO_2 increases the acidity of the solution and vice versa. This very careful balance is made more challenging by the fact that the cells produce 1 mole of CO_2 for every mole of O_2 consumed. dCO_2 will be measured by CO_2 sensors and an offline blood-gas analyzer. An acceptable range for dCO_2 is between 120 and 150 mmHg, with the ideal setpoint being 130 mmHg. If CO_2 is too low, sodium carbonate (Na_2CO_3) will be added and dissociated into CO_2 and H_2O in culture. Also, CO_2 gas can be sparged into the culture. Using Na_2CO_3 is more ideal because it eliminates issues with sparging rates

like shear stress. It can also form an ionic bond with lactic acid in solution to form sodium lactate ($NaC_3H_5O_3$), as seen by the chemical reaction below.

$$Na_2CO_3\ (s) + HC_3H_5O_3\ (aq.) \rightarrow NaC_3H_5O_3\ (aq.) + CO_2\ (g) + H_2O\ (l)$$

This helps remove lactate as a potential energy source over glucose for the cells. If the CO_2 is too high, either sterile air or pure O_2 will be sparged in more to strip the CO_2 from the medium.

pH levels are very heavily tied to dCO_2 and lactate levels, and cell growth is very sensitive to pH. Even a 0.1 deviation from the optimum value of 7.1 can affect glucose consumption and lactate synthesis. The culture medium in itself has sodium bicarbonate ($NaHCO_3$) to act as a buffering agent, however this alone is usually not enough to maintain tight control. The ideal pH setpoint is 7.1, although higher values are preferred during initial growth phase. This is because the initial cell growth phases produce a lot of lactate. pH probes will be used in the bioreactors for real-time measurements, however off-line measurements will also be performed since prolonged use of pH probes can result in reduced sensitivity. As lactate concentrations exceed the buffering capacity of the already present $NaHCO_3$, the pH becomes more acidic. To increase the alkalinity of the culture medium, a base such as NaOH is added, which subsequently also increases osmolality of the medium. It is important to tightly control addition of base, as the additive effects of high pH, high lactate concentrations, and high osmolality lead to an acceleration of cell death and slowing of growth. To counteract medium that is too alkaline, Na_2CO_3 will be added to dissociate into CO_2 and H_2O with a bonus effect of forming $NaC_3H_5O_3$, removing lactate as potential source of toxicity, delayed cell growth, and decreased product quality.

13.1.3 Inoculum Preparation - Large & Small Production Bioreactor Designs

Following recovery from cryogenic storage conditions, the CHO cells must be revived and acclimated to optimal culture conditions inoculation into seed and production bioreactors. Although cryogenic freezing maintains cell potential, the process of recovery is very harsh and the cells must undergo several cycles of replication before reaching a viable biomass that is compatible with aggressive volume scale-up strategies. Therefore,

the inoculum preparation steps are designed for small volumes and gentle culture conditions with ample nutrients and highly controlled atmospheric conditions.

13.1.3.1 250 mL Shaker Flask

To prepare the inoculum for cell seeding and growth, a 250mL Pyrex™ shaker flask with 125mL working volume will be filled with 95 mL of pre-warmed growth media via a serological pipette in a HEPA filtered hood on site. Fifty percent working volume allows for adequate agitation, aeration, and room for cell growth. Recombinant CHO DG44 cells will be recovered from cryogenic storage in a lab on site to a volume of 30 mL at a density of 3.00×10^5 cells/mL. The recovery procedure can be found in Appendix A. The 30mL of cells will be added via serological pipette to the pre-filled shaker flask to an initial density of 7.20×10^4 cells/mL. The flask will then be clamped to a flat, low speed orbital shaker at 60 rpm for agitation. The flask and shaker will be placed in a cell incubator at 36.5°C temperature and 5.0% CO_2 with built-in controls for 3 days to reach a desired cell concentration of 2.54×10^5 cells/mL. The culture will be sampled once daily to ensure control setpoints are being met. Media or feed supplement boluses will be injected to correct for any nutrient deficiencies. Since the flasks are in a CO_2 incubator, culture conditions will be altered accordingly if set point values are outside the desired ranges.

13.1.3.2 25 L Single-Use Bioreactor

To prepare for the next inoculation step, a 25L single-use, bag bioreactor with 12.5L working volume will be filled with sterile air and heated to 36.5°C with built-in controls. 12.4L of growth media will be transferred from a growth media storage tank to the bioreactor through jacketed pipe that contains 10% propylene glycol in water at 60°C in the outer annulus for heating. The transfer step will occur via peristaltic pump at a flow rate of 0.006 L/min. The rocking speed of the bioreactor will be initially set to 10 rpm at an angle of 6° and increased to 15 rpm and a 7°angle as media is added. After 1 hour of acclimating the media to the bioreactor, the cell culture from the shaker flask will be transferred via a peristaltic pump to the 25L bag bioreactor at a flow rate of 0.008 L/min.

The cell culture will be grown for 3 days. The culture will be sampled once daily to ensure control setpoints are being met and that nutrient levels are within the acceptable ranges. Media or feed supplement boluses will be injected to correct for any nutrient deficiencies. To correct for offsets in set points, the bag bioreactor conditions will be controlled as outlined in Section 13.1.2. The desired final cell density after 3 days is 8.95×10^3 cells/mL.

13.1.3 Bioreaction Processes - Large Production Bioreactor Design

The following sections outline the remaining upstream processes after inoculum preparation for the Large Production Bioreactor Process Scheme, ending in a 20,000 L stainless steel production bioreactor. The seed bioreaction steps grow the cells to a peak viable cell density, while the production bioreaction step maximizes mAb product formation at a consistent cell density.

13.1.3.1 100 L Single-Use Seed Bioreactor

For cell seeding, a 100L single-use, bag bioreactor with 50L working volume will be filled with sterile air and heated to 36.5°C with built-in controls. 37.5L of growth media will be transferred from a growth media storage tank to the bioreactor through jacketed pipe that contains 10% propylene glycol in water at 60°C in the outer annulus for heating. The transfer step will occur via peristaltic pump at a flow rate of 2.5 L/min. The rocking speed of the bioreactor will be initially set to 15 rpm at an angle of 6° and increased to 25 rpm and an 8° angle as media is added. After 1 hour of acclimating the media to the atmosphere of the bag, the 12.5L of cell culture from the 25L bioreactor will be transferred via a peristaltic pump to the 100L bag bioreactor at a flow rate of 0.83 L/min.
The cell culture will be grown for a total of 3 days. The culture will be sampled once daily to ensure control setpoints are being met and that nutrient levels are within the acceptable ranges. To correct for offsets in set points, the bag bioreactor conditions will be controlled as outlined in Section 13.1.2. The desired final cell density after 3 days is 1.18×10^4 cells/mL.

13.1.3.2 500 L Single-Use Seed Bioreactor - Two in Parallel

To continue cell growth, two 500L single-use, bag bioreactors with 250L working volumes will be filled with sterile air and heated to 36.5°C with built-in

controls. Initially, the bioreactors will be filled to half of their working volume. 100L of growth media will be transferred from a growth media storage tank to each bioreactor through jacketed pipe that contains 10% propylene glycol in water at 60°C in the outer annulus for heating. The transfer step will occur via a diaphragm pump at a flow rate of 6.7 L/min. The rocking speed of the bioreactor will be initially set to 5 rpm at an angle of 3° and increased to 15 rpm and a 4° angle as media is added. After 2 hours of acclimating the media to the bag, 25L of cell culture from the 100L bioreactor will be transferred via a peristaltic pump to each 500L bag bioreactor at a flow rate of 1.67 L/min.

The cell culture will be grown for a total of 3 days. Each day after the first day, a media bolus of 62.5L containing 3.00% by volume of CellBoost™ 7a and 0.30% by volume of CellBoost™ 7b will be added to each bioreactor. This helps maintain nutrient levels and prevent overcrowding. The culture will be sampled once daily to ensure control setpoints are being met and that nutrient levels are within the acceptable ranges. Media or feed supplement boluses will be injected to correct for any nutrient deficiencies. To correct for offsets in set points, the bag bioreactor conditions will be controlled as outlined in Section 13.1.2. The desired final cell density in each bioreactor after 3 days is 6.21×10^3 cells/mL.

13.1.3.3 2,000 L Single-Use Seed Bioreactor - Two in Parallel

After 3 days of culture, two single-use, 2,000 L bag bioreactors with 1,600L working volumes will be filled with sterile air and heated to 36.5°C with built-in controls. Initially, the bioreactors will be filled to only half of the final volume. 550L of growth media will be transferred from a growth media storage tank to each bioreactor through jacketed pipe that contains 10% propylene glycol in water at 60°C in the outer annulus for heating. The transfer step will occur via a diaphragm pump at a flow rate of 19.0 L/min. The agitation speed of the bioreactor will be initially set to 100 rpm and increased to 110 rpm as media is added. After 2 hours of acclimating the media to the atmosphere of the bag, 250L of cell culture from each 500L bioreactor will be transferred via a peristaltic pump to each 2,000L bag bioreactor at a flow rate of 16.7 L/min.

The cell culture will be grown for a total of 3 days. Each day after the first day, a media bolus of 400L containing 3.00% by volume of CellBoost 7a and 0.30% by volume of CellBoost 7b will be added to each bioreactor. This helps maintain nutrient levels and prevent overcrowding. The culture will be sampled once daily to ensure control setpoints are being met and that nutrient levels are within the acceptable ranges. Media or feed supplement boluses will be injected to correct for any nutrient deficiencies. To correct for offsets in set points, the bag bioreactor conditions will be controlled as outlined in Section 13.1.2. The desired final cell density in each bioreactor after 3 days is 5.12×10^3 cells/mL.

13.1.3.4 20,000 L Stainless Steel Stirred Tank Production Bioreactor

After cell seeding is complete, the final production bioreactor will grow the culture up to peak density and then maximize production formation and secretion from the cells. A 20,000L stainless steel, cylindrical bioreactor with pitch-blade impellers, a heating jacket, and sparging apparatuses for sterile air and sterile O_2 will be will be filled with sterile air and heated to 36.5°C using proportional–integral–derivative (PID) controllers. The agitation speed of the bioreactor's impeller power will be set to 0.055 W/kg and then adjusted as needed. Air will be sparged in at a rate of 0.019 volume of air per volume of liquid per minute (vvm), which assumes that only 30% of the sparged air is taken up by the cells. This calculation can be found in Appendix D. Initially, the bioreactor will be filled with media to only half of the final volume. 3,550L of growth media will be transferred from a growth media storage tank to each bioreactor through jacketed pipe that contains 10% propylene glycol in water at 60°C in the outer annulus for heating. The transfer step will occur via a peristaltic pump at a flow rate of 29.6 L/min. After 4 hours of acclimating the media to the tank conditions, 3,200L of cell culture from both 2,000L bioreactor bags will be transferred via a diaphragm pump to the production bioreactor at a flow rate of 26.7 L/min.

The total production duration is 19 days, over which growth media and feed supplements will be added each day to maintain nutrient levels and prevent overcrowding. Each subsequent day of production, a media bolus of 375L

containing 3.00% by volume of CellBoost 7a and 0.30% by volume of CellBoost 7b will be added to the bioreactor. The culture will be sampled once daily to ensure control setpoints are being met, that nutrient levels are within the acceptable ranges, and that mAb production is occurring at an acceptable rate. Media or feed supplement boluses will be injected to correct for any nutrient deficiencies. The bioreactor conditions will be controlled via PID control to keep pH, osmolality, sparging rates, mixing rates, dO_2, dCO_2, and venting within setpoints outlined in Section 13.1.2. The desired final cell density in the bioreactor after the first 12 days is 9.00×10^6 cells/mL, which is the specified peak viable cell density. For the remaining 7 days, mAb production will be maximized at a constant cell density to reach a final mass of 40.1 kg in a volume of 13,500L for a final titer of 2.97 g/L. At the end of the production period, the culture is transferred to a centrifuge for downstream primary recovery.

13.1.4 Bioreaction Processes - Small Production Bioreactor Design

The following sections outline the remaining upstream processes after inoculum preparation for the Small Production Bioreactor Scheme, ending in a 2,000 L single-use production bioreactor. As compared to the Large Production Bioreactor Design, this design only contains one seed bioreactor, because the final bioreactor volume is smaller. However, to ensure proper dilution ratio and scale up conditions, the cells are held for a longer time in this seed bioreactor. The seed bioreaction steps grow the cells to a peak viable cell density, while the production bioreaction step maximizes mAb product formation at a consistent cell density. The two designs use the same equipment for the inoculum stages, but this design only has two additional bioreactors after this: a 500L bioreactor which feeds the final 2,000L production bioreactor.

The following sections outline the remaining upstream processes after inoculum preparation for the Small Production Bioreactor Process Scheme, ending in a 2,000 L single-use bag production bioreactor.

13.1.4.1 500 L Single-Use Seed Bioreactor

This seed bioreaction step utilizes the same 500L single-use, bag bioreactor as described in Section 13.1.3.2, but the following changes will be made. 112.5 L of fresh cell culture media will be transferred from a media storage

tank to the bioreactor via peristaltic pump at a flow rate of 7.50 L/min. After 2 hours of acclimating the media to the bioreactor environment, 12.5 L of cells from the previous bioreactor will be transferred to the 500 L bioreactor via a peristaltic pump at a flow rate of 0.83 L/min. After the initial transfer step, a media bolus of 59.4 L containing regular growth media, CellBoost 7a, and 7b will be fed to the bioreactor daily for the remaining bioreaction period. The cell culture will be grown for 6 days to a final cell density of $3.09x10^4$. All other conditions and process steps including culture sampling and set point correction, are the same as described in Section 13.1.3.2.

13.1.4.2 2,000 L Single-Use Production Bioreactor

The production bioreactor process for optimal product formation utilizes the same 2000L bag bioreactor described in Section 13.1.3.3 with the following changes. Upon the start of the production period, the bioreactors will be filled to half of the total final volume with 580L of growth media. This volume will be transferred from a media storage tank to the bioreactor via a peristaltic pump at a flow rate of 18.4 L/min. After 2 hours of acclimating the media to the atmosphere of the bag, 250L of cell culture from the previous bioreactor will be transferred via a peristaltic pump to the 2,000L bag bioreactor at a flow rate of 13.3 L/min. A media bolus of 43.3 L containing regular growth media, CellBoost 7a, and 7b will be fed to the bioreactor daily for the remainder of the production period, which is 19 days. The desired final cell density after the first 12 days is $9.00x10^6$ cells/mL, which is the specified peak viable cell density. For the remaining 7 days, mAb production will be maximized at a constant cell density to reach a final mass of approximately 10.0 kg of mAb, with a final titer of 6.41 g/L. All other conditions and process steps including culture sampling and set point correction, are the same as described in Section 13.1.3.3. At the end of the production period of each bioreactor, the culture is transferred to a centrifuge for downstream primary recovery.

13.2 Downstream Purification Process Description

The mAbs are secreted from the cells grown in the upstream process. After this process is complete, the product must be separated from the cell mass and purified according to FDA

standards. The purification process is needed to remove process impurities such as host cell proteins, nucleic acids, and lipids. At the end of the upstream process, the protein titers are 2.97 g/L and 6.41 g/L for the Large and Small Production Bioreactor Designs, respectively. During the purification process, there are several volume reduction steps that will increase the protein titer. However, there is an upper limit for protein titer of 150g/L because at high titers, the protein aggregates solution becomes too viscous. The downstream process consists of three major parts: primary recovery, purification, and polishing steps. These steps are shown in the process flow diagrams in Sections 12.2 and 12.4.

13.2.1 Primary Recovery

The primary recovery steps consist of both centrifugation and depth filtration, which is used for the removal of cells and cell debris from the culture broth and clarification of the cell culture supernatant that contains the antibody product.

13.2.1.1 Centrifugation

Contents of the final production bioreactor are transferred into the centrifuge via a peristaltic pump. The centrifuge separates the extracellular product from the cells and other solid waste. Because the product is secreted, the cells are no longer needed for the process and they will be disposed of. Centrifugation operating conditions will be chosen to ensure the cells are not lysed because this would release additional contaminants in the product solution. It is assumed that the cells take up a negligible volume in the bioreactors, so the protein titer is constant for this step, with the large production bioreactor design having a protein titer of 2.97 g/L of solution and the small production bioreactor design having a protein titer of 6.41 g/L of solution.

The centrifuge operates in a continuous manner, processing 4,000 L/hr for the large production bioreactor design and 780 L/hr for the small production bioreactor design. It is operated at 25°C and has a product yield of 96% with about 4% of desired product being discarded in the solid waste stream. Centrifugation for the Large Production Bioreactor Design will require a time of 4 hours and an additional 2 hours for CIP and SIP. Centrifugation for the Small Production Bioreactor Design will require a time of 2 hours and an additional 2 hours for CIP and SIP.

13.2.1.2 Depth Microfiltration

In addition to centrifugation, depth filtration will be used as a second recovery step to eliminate large solid particles from the media. A depth filter is used because there is a limit to the particle size that can be removed by centrifugation. Similar to centrifugation, it will be assumed that the volume reduction from this step is negligible, keeping the protein titer constant. The supernatant from the centrifuge is applied to the filters. The feed will be filtered at a speed of 21 L/min/m^2 with a yield of 97%. For the Large Production Bioreactor Design, it will take 9 hours and for the Small Production Bioreactor Design, it will take 1.5 hours.

13.2.2 Initial Purification

The purification steps include the Protein A chromatography and cation exchange chromatography, with a diafiltration unit separating them. These units are used as a capture step in separating the product from smaller impurities and as a concentration step in reducing the overall volume.

13.2.2.1 Buffer Preparation

Many downstream unit operations, including the chromatography columns, will require various buffers to be prepared for each batch. Buffers will be purchased from Millipore Sigma and mixed with WFI in single-use storage containers. Single use containers will help minimize cleaning and sterilization procedures and reduce contamination. Once prepared, the pH and conductivities of the buffers will be checked and controlled until the buffers are used.

13.2.2.2 Protein A Chromatography

Protein A Chromatography is the first of three chromatography steps in the downstream process. It aims to isolate the mAb product by using a resin that selectively binds the IgG molecule. Protein A is *Staphylococcus aureus* cell wall protein that binds selectively to the Fc region of IgG. Protein A contains five regions that bind to the Fc region of IgG and one molecule of protein A (on a resin matrix) can bind at least two molecules of IgG. It is a naturally occuring on the gram-positive bacterium, and it has been engineered for protein purification applications[19]. This step is used to remove process-related impurities such as host

cell proteins, DNA, cell culture media components, and endogenous and adventitious virus particles with a high purity and yield. The MabSelect SuRe LX media resin chosen for this process consists of an alkali- and protease stabilized, recombinant protein A ligand coupled to a rigid, agarose matrix. The stability of the protein A ligand minimizes ligand leakage and allows for cleaning procedures based on NaOH. In addition, the highly cross-linked agarose matrix of the resin enables the use of high flow velocities at production scale.[20]

This operation is the first volume reduction step in the downstream process. Once the protein has been loaded onto the column, it will be eluted with a smaller volume in order to concentrate the product. For the Large Production Bioreactor Design, the working volume will be reduced from 13,500L to 3,200L. For the Small Production Bioreactor Design, the working volume will be reduced from 1,560L to 750L. This increases the protein titer to 10.7 g/L and 11.5 g/L, respectively.

Before the harvest cell culture fluid is passed over the column, the column is equilibrated with 5 column volumes (CV) of equilibration buffer (20 mM sodium phosphate, 150 mM NaCl at a pH of 7.4). After this step, the filtrate from the depth filtration is loaded onto the column. Then, there are two wash steps that wash away any impurities that are not bound to the resin. The first wash step uses 3.5 CVs of an equilibration buffer and the second wash step uses 1 CV of a wash buffer (50 mM acetate at a pH of 6). The mAbs are then washed from the column using 4 CVs of an elution buffer (50 mM acetate at a pH of 3.5). The low pH allows for the removal of the product as well as inactivation of viruses present in the solution. The elution stream is collected and transferred to a storage tank. The column is regenerated using 3 CV of buffer (100 mM sodium acetate, pH 2.9) and CIP uses 4 CVs of 100 mM NaOH. Following CIP, the SIP will be performed after each batch.[21] The column is expected to produce a 92% yield with a 98% purity. For the Large Production Bioreactor Design, it will require 19 hours to process all of the input, which will be processed in 4 cycles. For the Small Production Bioreactor Design, it will require 4 hours to process each input, which will require one cycle.

13.2.2.3 Virus Inactivation

CHO cells used to manufacture the mAbs produce endogenous retroviruses and are occasionally infected with adventitious viruses during processing. The best approach to ensure adequate viral clearance is to have multiple, orthogonal virus-removal steps and at least one virus inactivation steps. Virus inactivation methods include low pH, heat, irradiation, and chemical agents. For this process, the method for inactivating the viruses will be holding the solution in a low pH buffer. This method was chosen because it can be combined with the elution step from the Protein A chromatography column to create a more integrated process. The product will be eluted from the column with an low pH buffer and once all of the eluent has been collected, the solution will be held for 2 hours before starting diafiltration. This time will allow the viruses to be inactivated in the acidic conditions.[22]

13.2.2.4 Ultrafiltration / Diafiltration (UF/DF)

Ultrafiltration and diafiltration are size-exclusion, pressure-driven membrane processes used for protein concentration and buffer exchange. The desired separation is created by the different filtration rates of the various species and the applied pressure driving force. Solvent, buffer salts, and other small molecules migrate through the membrane while the protein is retained. The ultrafiltration will be carried out in the tangential flow filtration (TFF) mode. Tromethamine (Tris base) (pKa = 8.1) will be added to the retentate system at the same rate that filtrate is removed. This will ensure the protein is in a new buffer to prime the product for the next chromatography step.

The UF/DF process will be run continuously using membrane cassettes totaling 2.5 m^2 in area and with a pore size of 30 kDa. The product in the large production bioreactor design will be concentrated from 10.7 g/L to 52.1 g/L. The product in the small production bioreactor design will be concentrated from 11.5 g/L to 55.4 g/L. The total processing time for the Large Production Bioreactor Design will be 4 hours and 1.5 hours for the Small Production Bioreactor Design.

13.2.2.5 Cation Exchange Chromatography

Cation exchange chromatography uses a resin modified with negatively charged functional groups to bind positively charged proteins. For this process, Capto S resin will be used, which has a $-SO_3$ functional group. It is typically used for mAbs with neutral to basic pI values. Because the pI of the protein is 9.2, it will be positively charged at its working pH of 5.5. The antibody is bound onto the resin during the loading step and eluted with a increasing salt buffer, while keeping pH constant. The increased salt concentration causes the sodium cations to exchange with mAb. The most negatively charged impurities are removed during the load and wash steps. These impurities include DNA, some host cell protein, and leached protein A.[23]

First, the column is packed with the resin and equilibrated using 5 CV of 20 mM sodium acetate buffer. Then, the sample is loaded with the filtrate from the previous diafiltration step. The wash step uses 5 CV of 20 mM sodium acetate buffer. The product is then eluted with 2 CV of a buffer consisting of 20 mM sodium acetate with 0.5M sodium chloride and collected for additional purification. The column is regenerated using 2 CVs of 20 mM sodium acetate with 1M sodium chloride and CIP is performed with 3 CV of 0.5 M NaOH. The column is expected to have a 92% yield. For the Large Production Bioreactor Design, it will require 16 hours to process all of the input, which will be processed in 4 cycles. For the Small Production Bioreactor Design, it will require 4 hours to process each input, which will require one cycle. Similar to the Protein A chromatography column, the volume of the product solution is determined by the elution step. However, for this column, there will be an increase in the volume because of the volume required to remove the protein from the resin. The Large Production Bioreactor Design will have a volume increase from 640 L to 1290 L and the Small Production Bioreactor Design will have an increase from 150 L to 320 L. At this point, the protein titers for the two designs are 30.7 g/L and 24.0g/L, respectively.

13.2.3 Polishing Steps

The polishing steps consist of virus filtration, hydrophobic interaction chromatography, and two final filtration steps (ultrafiltration/diafiltration and sterile filtration). These steps are used to remove viruses, aggregated protein, and any other impurities before storing the proteins.[28] The same processes will be used in the downstream process for both upstream schemes, but they will be adjusted in capacity. At various points in the downstream purification process, the product will be checked to ensure quality standards are met.[24]

13.2.3.1 Virus Filtration

The virus filtration step is used to remove the virus particles that were previously inactivated. For safety requirements, the product must contain less than one virus particle per million doses, which translates to 12-18 $\log_{10}$ clearance of endogenous retroviruses and 6 $\log_{10}$ clearance for adventitious viruses. The US Food and Drug Administration (FDA) requires that manufacturers of biotech products that use murine cell lines (including CHO cells) are to demonstrate the clearance capability of their manufacturing processes with one relevant retrovirus. Because the virus particles have a diameter of 18–26 nm, but a typical monoclonal IgG antibody has a hydrodynamic diameter of 8–12 nm, filters are required to have a very narrow pore size distribution to achieve a high clearance and yield.[25]

Four filters will be used and the filtration unit can be run continuously in four cycles during which the hollow-fiber membrane will retain the virus waste. This will take 10 hours for the Large Production Bioreactor Design and 6 hours for the Small Production Bioreactor Design.

13.2.3.2 Hydrophobic Interaction Chromatography

Hydrophobic interaction chromatography (HIC) is commonly used as a polishing step in mAb purification processes. It is an effective step for removing trace product and process-related impurities such as aggregates. It is important to remove protein aggregates because they may lead to an immunogenic reaction when administered to the patient.[26] HIC is a tool used to separate proteins based on their hydrophobicity. For this process, it will be run in flow through mode,

meaning the product will flow through while the impurities bind to the resin. These impurities have chemical properties very similar to the target but they will be more hydrophobic than the target protein. They will bind at relatively low salt concentrations to the resin, while the mAb will not bind unless there is a high salt concentration.[27] Depending on the mAb product, HIC may not be required if cation exchange can adequately purify the product. If only two chromatography steps are required, this step can be easily eliminated.

The column is equilibrated with 5 CVs of 1.3 M ammonium sulfate, 50 mM sodium phosphate, adjusted to pH 7 using 1M tris base and conductivity adjusted to 110mS/cm using ammonium sulfate. The filtrate from the virus filtration unit is loaded onto the column. The product pool is then collected, with a pH of 7 upon elution, and is quenched with 1M acetic acid to a final pH of 5.5 prior to analysis. The column is then washed with 5 CV of equilibration buffer. The resin is cleaned with 5 CVs of WFI followed by 5 CVs of 1 M NaOH. The column is expected to have a 92% yield. For the Large Production Bioreactor Design, it will require 13 hours to process all of the input, which will be processed in 4 cycles. For the Small Production Bioreactor Design, it will require 7 hours to process each input, which will require one cycle. This chromatography step will result in an increase in the working volume so the protein titer will decrease from 22.6 g/L to 7.7 g/L for the large production bioreactor design and from 22.8 g/L to 3.2 g/L for the small production bioreactor design.

13.2.3.3 Ultrafiltration / Diafiltration (UF/DF)

A second UF/DF process will be run to achieve the final desired protein concentration and resuspend the protein in sterile PBS.[28] Similar to the first UF/DF, the filtration will be performed in the tangential flow mode and will concentrate the product from 7.7 g/L to 37.0 g/L and suspend the product protein in PBS in preparation for the final product sterilization.

13.2.3.4 Sterile Filtration

Sterile filtration serves as the last purification step to remove any final contaminants. The product will be directly filtered into the final storage containers using a 0.2 um membrane cartridges to ensure sterility. For the Large Production

Bioreactor Design, 70 filters will be run in parallel, one for each of the final storage containers, and it will take 3 hours to process all input. For the Small Production Bioreactor Design, 42 filters will be run in parallel and it will also take 3 hours to process all input. The filters are expected to recover 97% of the product.

13.2.3.5 Final Storage

The purified product will be stored in 10 L polycarbonate Nalgene biotainers at -80°C. The product will be stored in bulk current market. Depending on the demand, the product will be sent to the formulation group who will package the mAbs for patient use in the correct dosage. 70 bottles will be used for the Large Production Bioreactor Design and 42 will be used for the Small Production Bioreactor Design. The product will be stored at a titer of 36 g/L and 15 g/L for the two designs.

14. Energy Balance and Utility Requirements

The major utility requirements for this process are electricity and steam. It is assumed that since this plant is part of a larger operation, utility supply systems are already installed. The utility consumption is the only cost consideration.

The Large Production Bioreactor scheme requires 79,300 kWh of electricity. At the PECO (Philadelphia Electric Company) rate of $0.085/kWh, this results in a per batch cost of $6,740 [28]. Steam is another heavily used utility, at $0.02/kg resulting in a $5,007 expenditure. A large portion of these utilities will be used for operating the large 20,000 L bioreactor, as well as for CIP and SIP processes. The Small Production Bioreactor scheme, therefore, requires much less electricity and steam in the upstream process, since the maximum bioreactor size is 2,000 L and no CIP/SIP is required since all units are disposable. The total utility cost for the small bioreactor scheme is $6,600 which is less than half that of the large bioreactor scheme.

15. Equipment List and Unit Descriptions

15.1 Upstream Production Process Units

The equipment used in the two designs (Large and Small Production Bioreactor) are described in the following sections. Each section references the unit in the process flow sheets from Section 12. The equipment used for the two designs will be similar, but will be adjusted based on volumes.

15.1.1 Large Production Bioreactor Design

15.1.1.1 Blending Tank (PFD 01/P-1)

This blending tank is used to mix ActiPro dry powder media with WFI before being filtered and then transferred to a storage tank until further use. The tank will be manufactured from polyethylene with a volume of 75L, a working capacity of 80%, and a height to diameter ratio of 2 to 1. Clean-in-place (CIP) and Steam-in-place (SIP) will be conducted after each batch, the procedures for which can be found in Appendix C. The tank operates at room temperature and 1 bar. The tank is manufactured by White Mountain Process and costs $12,500.

15.1.1.2 Dead-End Filter (PFD 01/P-3)

This dead-end filter is used to filter and remove large contaminants from blended media before being transferred to storage until further use. The filter pore size is 0.2 µm and the filtration area is 0.57 m^2. The membrane filter material is polyethersulfone (PES) with a polyethylene film edge and polyester supports. The maximum differential pressure at room temperature is 6.9 bar with a throughput of 2000 $L/m^2/h$. The filters are sterile, disposable, and come in disposable housing units, which are replaced after every batch. Filter P-19 is connected to blending tank P-1 for filtration of ActiPro media. The capsules are manufactured by Millipore Sigma and cost $400.

15.1.1.3 Storage/Blending Tank (PFD 01/P-5)

This storage tank is used to store blended and filtered ActiPro culture media at 4°C until being transferred to the 250mL Shaker Flask, 25L Single-Use Bioreactor, and 100L Single-Use Seed Bioreactor. The tank will be manufactured from polyethylene with a volume of 75L, a working capacity of 80%, and a height to diameter ratio of 2 to 1. Clean-in-place (CIP) and Steam-in-place (SIP) will be

conducted after each batch, the procedures for which can be found in Appendix C. The tank operates at 4°C via electric cooling and 1 bar. The estimated cost of the storage tank is $12,500.

15.1.1.4 250 mL Shaker Flask with Orbital Shaker & Incubator (PFD 01/P-7)

A baffled 250 mL shaker flask manufactured by Corning is used for the first inoculum preparation step after cryogenic recovery of the cells (Appendix A). The flask is made from Pyrex and must be autoclaved at 121°C for 60 minutes before use. The flask will be placed on a low speed orbital shaker with a flat platform manufactured by Corning LSE. The orbital shaker is 25.5 cm long, 32.0 cm wide, and 16.0 cm in height, with maximum speed of 60 rpm. The flask and shaker apparatus will be placed inside an Thermo Scientific Forma Series 3 Water Jacketed CO_2 Incubator. The incubator comes equipped with temperature, CO_2, O_2, and humidity controls. The incubator is manufactured from stainless steel with inner dimensions 54.1 cm in length, 68.1 cm in width, and 50.8 cm in height. The incubator will be set to 36.5°C, 1 bar, a pH of 7.1, 5.0% CO_2, and 40% dO_2. The process time for the shaker flask, orbital shaker, and incubator is 3 days. The shaker flasks are purchased in quantities of six for $157.80 from Corning. The orbital shaker is a one-time purchase from Corning for $900.00. The incubator is also a one-time purchase from Thermo Fisher Scientific for $7,900.

15.1.1.5 25 L Single-Use Bioreactor (PFD 01/P-9)

The second inoculum preparation step uses the single-use ReadyToProcess WAVE™ 25 L rocking bioreactor system from GE Healthcare Life Sciences. The system consists of a rocker, CBCU gas mixers, pumps, and disposable, pre-sterilized, 22L Cellbags for cell expansion and growth in suspension. It is also equipped with high level sensors and stable, automated control for temperature, liquid transfer, dO_2, and pH. Cellbags are easily attachable and all operations are managed with the accompanying UNICORN software installed on a computer. The base unit dimensions are 0.40 m long, 0.21 m wide, and 0.56 m high. The tray dimensions to hold the Cellbag are 0.8 m long, 0.07 m wide, and 0.61 m high. The rocker allows for temperature control integrated into the base unit, stable mixing, and real-time load measurements. Rocking also helps maintain dissolved

oxygen levels. The CBCU delivers gases to the culture and is connected to optical sensors in the cell bag bioreactor for online pH and dO_2 control. A maximum of two CBCU gas mixers and three pump units can be connected to the main rocker. Because the cell bags are pre-sterilized and disposable, there are no CIP or SIP steps required and there is minimal cross-contamination between batches. The cell bags are manufactured from clear, multilayer, laminated USP Class VI plastics and are replaced between each batch. The unit is kept at 36.5°C, 21 bar, pH at 7.1, and 40% dO_2. The rocker is set to a final agitation speed of 15 rpm at a 7° angle. The process time for the unit is 3 days. The rocker and CBCU gas mixer are purchased from GE Healthcare Life Sciences for $60,000 and $1,000, respectively. The disposable 22L Cellbag is purchased for $500.00.

15.1.1.6 100 L Single-Use Seed Bioreactor (PFD 01/P-29)

Cell seeding and scale-up uses the single-use ReadyToProcess WAVE Bioreactor 200 system. The system consists of a rocker base unit and a disposable, pre-sterilized 100L Cellbag. It is also equipped with high level sensors and PID control for aeration, temperature, dO_2, and pH. All operations are managed with the accompanying UNICORN software installed on a computer. The unit dimensions including the Cellbag are 1.85 m long, 1.10 m wide, and 1.12 m high. The rocker produces a wave-like motion that mixes the culture, suspends the cells, and helps provide effective oxygen transfer from the bioreactor headspace. The degree of mixing and oxygen transfer will be controlled by adjusting the rocking speed and angle. Oxygen transfer is also supplied by an internal air pump that passes air through the headspace to continuously supply oxygen and strip waste gases. O_2 is also connected to a separate port to mix air with O_2 if necessary. dO_2 levels are controlled either by altering the concentration of O_2 in air pumped into the headspace or by altering rocking speed or angle. A configured dO_2 system with a sensor provides control for both of these options. On the underside of the rocker is a heating plate that controls temperature along with a temperature sensor inserted into the Cellbag. An electrochemical pH probe measures online pH and is connected to pumps for addition of Na_2CO_3 in H_2O for acid or NaOH in H_2O for base. Because the cell bags are pre-sterilized and

disposable, there are no CIP or SIP steps required and there is minimal cross-contamination between batches. The cell bags have a 50% working volume, are manufactured from clear, multilayer, laminated USP Class VI plastics, and are replaced between each batch. The maximum operating pressure is 0.1 bar, and the recommended operating pressure is 5 to 7.5 mbar. The unit is kept at 36.5°C, 0.007 bar, pH at 7.1, and 40% dO_2. The final rocking speed is set to 25 rpm at an 8° angle. The process time for the unit is 3 days. The rocker and 100L CellBag are purchased from GE Healthcare Life Sciences for $90,000 and $800, respectively.

15.1.1.7 Blending Tanks (PFD 01/P-11; P-17; P-23)

Blending tank P-22 is identical to the unit described in 15.1.1.1, but has a volume of 4,000L and costs $51,000.

Blending tank P-17 is identical to the unit described in 15.1.1.1, but it is used to mix feed supplement CellBoost™ 7a dry powder media with WFI before being filtered and transferred to a storage tank until further use. The tank will have a volume of 7,000L and cost $63,200.

Blending tank P-23 is is identical to the unit described in 15.1.1.1, but it is used to mix feed supplement CellBoost™ 7b dry powder media with WFI before being filtered and transferred to a storage tank until further use. The tank will have a volume of 700L and cost $24,300.

15.1.1.8 Dead-End Filters (PFD 01/P-13; P-19; P-25)

These dead-end filters are the same as previously described in Section 15.1.1.2, connected to blending tanks P-11, P-17, and P-23, respectively.

15.1.1.9 Storage/Blending Tanks (PFD 01/P-15; P-21; P-27)

Storage tank P-15 is identical to the unit described in 15.1.1.3, but has a volume of 4,000L and is used to store blended and filtered ActiPro culture media at 4°C until being transferred to the 500L and 2,000L Single-Use Seed Bioreactors. The tank costs $51,000.

Storage tank P-21 is identical to tank P-15, but stores blended and filtered feed supplement CellBoost 7a media and has a volume of 250L. The storage tank costs $18,000.

Storage tank P-27 is identical to P-21 is but stores blended and filtered feed supplement CellBoost 7b media and has a volume of 25L. The storage tank costs $9,200.

15.1.1.10 500 L Single-Use Seed Bioreactors (PFD 01/P-32,33)

Cell seeding continues with use of another single-use ReadyToProcess WAVE Bioreactor 500/1000 system. The system consists of a rocker base unit, and a disposable, pre-sterilized 500L Cellbag. It is also equipped with high level sensors and PID control for aeration, temperature, dO_2, and pH. All operations are managed with the accompanying UNICORN software installed on a computer. The unit dimensions including the Cellbag are 2.26 m long, 1.24 m wide, and 1.60 m high. The rocker produces a wave-like motion that mixes the culture, suspends the cells, and helps provide effective oxygen transfer from the bioreactor headspace. The degree of mixing and oxygen transfer will be controlled by adjusting the rocking speed and angle. Oxygen transfer is also supplied by an internal air pump that passes air through the headspace to continuously supply oxygen and strip waste gases. O_2 is also connected to a separate port to mix air with O_2 if necessary. dO_2 levels are controlled either by altering the concentration of O_2 in air pumped into the headspace or by altering rocking speed or angle. A configured dO_2 system with a sensor provides control for both of these options. On the underside of the rocker is a heating plate that controls temperature along with a temperature sensor inserted into the Cellbag. An electrochemical pH probe measures online pH and is connected to pumps for addition of Na_2CO_3 in H_2O for acid or NaOH in H_2O for base. Because the cell bags are pre-sterilized and disposable, there are no CIP or SIP steps required and there is minimal cross-contamination between batches. The cell bags have a 50% working volume, are manufactured from clear, multilayer, laminated USP Class VI plastics, and are replaced between each batch. The maximum operating pressure is 0.1 bar, and the recommended operating pressure is 5 to 7.5 mbar. Each unit is kept at 36.5°C, 0.007 bar, pH at 7.1, and 40% dO_2. The final rocking speed is set to 15 rpm at an 4° angle. The process time for the unit is 3 days. Each rocker and 500L CellBag

are purchased from GE Healthcare Life Sciences for $150,000 and $1,000, respectively. Two rockers and CellBags are required per batch.

15.1.1.11 2,000 L Single-Use Seed Bioreactors (PFD 01/P-36,37)

The last cell seeding step is performed with use of another single-use system, the Xcellerex XDR-2000 cell culture bioreactor systems from GE Healthcare Life Sciences. The system consists of a jacketed bioreactor vessel, an I/O and gas mixing cabinet, a control console, and a bioreactor bag assembly,. The jacketed vessel, manufactured from 304 grade stainless steel, provides temperature control via an external temperature control (PID) unit. It has a height to diameter aspect ratio of 1.5 to 1. The vessel also has built in load cells for weight measurement, inlet and exhaust filter holders, and sidewall ports. The sidewall ports allow for sterile sampling and sterile probe insertion for pH, dO_2, dCO_2 and temperature measurements. The I/O cabinet houses probe transmitters and peristaltic pumps, while the gas management cabinet houses mass flow controllers for delivery of gases to the bag sparger or headspace. The control console visualizes all measurements and manages controls of the Xcellerex XDR system. The bag assembly consists of a bioreactor bag incorporated with an impeller/sparger assembly mounted on the bottom for efficient mixing and oxygen transfer. The impeller is magnetically coupled, has 4 blades at a pitch of 40°, and the impeller diameter to bag diameter aspect ratio is 0.34. The assembly is also comprised of tubing, complete with weldable and aseptic connectors for liquid transfer, a disposable pressure sensor, and filters for inlet, exhaust, and headspace gas transfer. The bag itself has a 100% working volume of 2,000L, is manufactured from clear, multilayer, laminated USP Class VI plastics, and is replaced between each batch. Because the bags are pre-sterilized and disposable, there are no CIP or SIP steps required and there is minimal cross-contamination between batches. The maximum operating pressure is 0.05 bar. Each unit is kept at 36.5°C, 0.007 bar, pH at 7.1, and 40% dO_2. The agitation speed is set to 110 rpm. The process time for the unit is 3 days. Each Xcellerex XDR vessel and 2,000L Probag are purchased from GE Healthcare Life Sciences for $250,000 and $5,000, respectively. Two vessels and Probags are required per batch.

15.1.1.12 Blending Tank (PFD 01/P-46)

Blending tank P-46 is identical to the first unit described in 15.1.1.1 for mixing regular ActiPro growth media, but has a volume of 6,000L and costs $59,400.

15.1.1.13 Dead-End Filters (PFD 01/P-48)

These dead-end filters are the same as previously described in Section 15.1.1.2, connected to blending tank P-48.

15.1.1.14 Storage/Blending Tanks (PFD 01/P-50; P-41; P-44)

Storage tank P-50 is identical to the first unit described in 15.1.1.9, but has a volume of 6,000L and costs $59,400.

Storage tank P-41 is identical to the second unit described in 15.1.1.9, but has a volume of 7,500L and costs $69,400.

Storage tank P-44 is identical to the third unit described in 15.1.1.9, but has a volume of 750L and costs $25,500.

15.1.1.15 20,000 L Stainless Steel Production Bioreactor (PFD 01/P-52)

The mAb production step is performed with a traditional stainless-steel, custom, jacketed bioreactor with a 20,000 L volume and a 16,000 L working volume. The tank is cylindrical, with a height to diameter ratio is 2 to 1. The bioreactor is equipped with an impeller, which has a total diameter that is 1/3 the diameter of the tank. Each impeller blade is 1/5 the diameter of the impeller in height, and 1/4 the diameter of the impeller in width. There are 4 blades on the impeller at an angle of 40°. The bioreactor is also equipped with gas sparging elements and filter ports for sterile air and O_2, along with mass flow ports and filters for fed-batch media and feed supplement transfers, anti-foaming agent, aqueous Na_2CO_3, and aqueous NaOH. The vessel will be heated by a water-jacket. There will also be aseptic vessel ports for pH, dO_2, dCO_2, and temperature probes, in addition to sampling ports for daily cell density and viability measurements. The exhaust port will contain a filter and heater to prevent condensation. All set points will be controlled with PID controls. Following each batch, CIP and SIP will be conducted to sterilize the vessel. The vessel is operated at 36.5°C, 2 bar, pH at 7.1, and 40% dO_2. The specific agitation power is 0.055

W/kg, and air is sparged at 0.00981 vvm assuming that 30% of all sparged air is taken up by the cells. This calculation can be found in Appendix D. The process time for the unit is 19 days. The estimated total purchase cost of the vessel is $1,500,000.

15.1.2 Small Production Bioreactor Design

15.1.2.1 Blending Tank (PFD 03/P-1)

This blending tank is identical to the unit described in 15.1.1.1 for mixing regular ActiPro growth media, but has a volume of 300L and costs $18,100.

15.1.2.2 Dead-End Filter (PFD 03/P-3)

This dead-end filter is identical to the unit described in 15.1.1.2 and is connected to blending tank P-1.

15.1.2.3 Storage/Blending Tank (PFD 03/P-5)

This storage tank is identical to the unit described in 15.1.1.3, but has a volume of 300L and costs $18,100.

15.1.2.4 250 mL Shaker Flask with Orbital Shaker & Incubator (PFD 03/P-7)

This shaker flask is identical to the unit described in 15.1.1.4.

15.1.2.5 25 L Single-Use Bioreactor (PFD 03/P-9)

This 25L Single-Use WAVE Bioreactor from GE Healthcare Life Science is identical to the unit described in 15.1.1.5.

15.1.2.6 Blending Tanks (PFD 03/P-11; P-17)

Blending tank P-11 is identical to the second unit described in 15.1.1.7 for mixing CellBoost 7a media, but has a volume of 900L and costs $26,000.

Blending tank P-17 is identical to the third unit described in 15.1.1.7 for mixing CellBoost 7b media, but has a volume of 90L and costs $12,700

15.1.2.7 Dead-End Filters (PFD 03/P-13; P-19)

These dead-end filters are identical to the unit described in 15.1.1.2 and are connected to blending tanks P-11 and P-17, respectively.

15.1.2.8 Storage/Blending Tanks (PFD 03/P-15; P-21)

Storage tank P-15 is identical to the second unit described in 15.1.1.7 for CellBoost 7a storage, but has a volume of 50L and costs $10,700.

Storage tank P-21 is identical to the third unit described in 15.1.1.7 for CellBoost 7b storage, but has a volume of 25L and costs $9,100.

15.1.2.9 500 L Single-Use Seed Bioreactor (PFD 03/P-23)

This 500L Single-Use WAVE Bioreactor from GE Healthcare Life Sciences is identical to the unit described in 15.1.1.6. The operating time for this unit is 6 days. Only one rocker and 500L CellBag will be purchased for $150,000 and $1,000.

15.1.2.10 Blending Tank (PFD 03/P-31)

Blending tank P-31 is identical to the unit described in 15.1.1.1 for mixing regular ActiPro growth media, but has a volume of 1,100L and costs $28,200.

15.1.2.11 Dead-End Filter (PFD 03/P-33)

This dead-end filter is identical to the unit described in 15.1.1.2 and isconnected to blending tanks P-31.

15.1.2.12 Storage/Blending Tanks (PFD 03/P-35; P-26; P-29)

Storage tank P-35 is identical to the 15.1.1.3 for ActiPro growth media storage, but has a volume of 1,100L and costs $28,200.

Storage tank P-26 is identical to the first unit described in 15.1.2.8 for CellBoost 7a storage, but has a volume of 850L and costs $25,600.

Storage tank P-26 is identical to the first unit described in 15.1.2.8 for CellBoost 7b storage, but has a volume of 90L and costs $12,700.

15.1.2.13 2,000 L Single-Use Production Bioreactors (PFD 03/P-37)

This 2000L single-use Xcellerex XDR-2000 cell culture bioreactor system from GE Healthcare Life Sciences is identical to the unit described in 15.1.1.11. Only one rocker and 2,000L Probag will be purchased for $250,000 and $2,500.00, respectively.

15.2 Downstream Purification Process Units

The equipment used in for the downstream operations are described in the following sections. Each section references the unit in the process flow sheets from Section 12. The equipment used will be based on the corresponding upstream design and the differences are noted below.

15.2.1 Primary Recovery

15.2.1.1 Centrifuge (PFD 02/P-54, PFD 04/P-39)

The contents of the production bioreactor must be separated into a solid waste stream and liquid stream containing the desired product. A disc-stack centrifuge produced by GEA is used. The CSE 170 model, constructed with Stainless Steel 316, will be used for the large production bioreactor design and can be purchased for $1,500,000. It can process throughputs of 3,000-6,000 L/h. For the small production bioreactor scheme, a smaller centrifuge (CSC 20) will be used, which can process 500-1000L/hr. It will be purchased from GEA for $1,200,000. The unit operates in a continuous manner and will process all the contents of the production bioreactor immediately following its completion. After each batch, the unit will be sterilized with CIP and SIP. The unit operates at 25°C.

15.2.1.2 Storage Tank 6 (PFD 02/P-56, PFD 04/P-41)

This storage tank will be used to collect the liquid contents of the centrifuge and store it so that batches can be sent for further purification. It will be sized to match the size of the production bioreactor. For the large production bioreactor, the storage tank will have a volume of 20,000 L and for the small production bioreactor, will be 2,000 L. The maximum working capacity will be 80%. CIP and SIP will be conducted after each upstream batch is processed. The 20,000L tank will be purchased for $104,700 and the 2,000L tank for $36,000

15.2.1.3 Depth Filtration Unit (PFD 02/P-58, PFD 04/P-43)

Depth filtration is used to further clarify the solution containing the mAbs after centrifugation. The unit housing can hold up to 30 filters at once. For the large production bioreactor, the three rack housing will be used with 30 filters running per cycle. For the small production bioreactor, 10 filters will be used per cycle. The unit is purchased from Millipore Sigma and each filter costs $750. The housing unit for the 30 filter costs unit costs $67,300 and the housing unit for the 10 filters costs $29,200. The model is the Millistak+® Multilayer Process Scale Pod Filter with X0HC media. This filter media is meant for secondary clarification (post-centrifugation) and was chosen based on the specifications of the mAb product. The Pod filter system was chosen because it can easily scale

depending on the batch size by adding more or less filters. In addition, the filters are disposable, which eliminates the need for CIP. It has a maximum operating pressure of 3.5 bar at 25 °C and has a recommended feed flow rate of 21 $L/min/m^2$.

15.2.1.4 Storage Tank 7 (PFD 02/P-60, PFD 04/P-45)

This storage tank will collect the filtrate from the depth filtration unit and store it until it needs to be passed to the Protein A chromatography column in the correct. The unit has a capacity of 80% and is 20,000L for the large production bioreactor and 2,000L for the small production bioreactor design. The 20,000L tank will be purchased for $104,700 and the 2,000L tank for $35,900.

15.2.2 Initial Purification

15.2.2.1 Protein A Chromatography Column (PFD 02/P-62 PFD 04/P-47)

The Protein A affinity chromatography column is used to further purify the filtrate and isolates the product by selectively binding the mAbs. The Chromaflow 1000/100-300 column will be purchased from GE Healthcare for $250,000. The column is made with 316 Stainless Steel and is packed with MabSelect Sure LX resin, which can be be purchased from GE Healthcare Life Sciences for $8,000 per liter. The column operates as a packed bed, which will have a bed height of 0.25m and diameter of 1 m. The bed volume is 200 L and the resin has a binding capacity of 50 g mAb/L. The amount of resin required is determined by the binding capacity of the resin. For this process, 9.8 kg mAb are purified per Protein A chromatography cycle and this value is determined by (50g/L)*(200L bed volume) to get a maximum value of 10 kg mAb. The binding capacity of the resin decreases slightly after each run, but it was determined that 50 g/L is an accurate estimate of the average binding capacity. The resin can be used for 150-200 cycles and will be re-purchased every five years. The operating linear velocity used will be 250-400 cm/hr, depending on the buffer being used. For the large production bioreactor design, four cycles of Protein A chromatography are required. For the small production bioreactor, one cycle of Protein A chromatography is required for each 2,000 L bioreactor.

15.2.2.2 Storage Tank 8 (Virus Inactivation) (PFD 02/P-64, PFD 04/P-49)

This storage tank will be used to store the output from the Protein A column and is the mixing tank where the virus inactivation occurs. The unit will have a volume of 5,000L for the large production bioreactor design and 1,000L for the small production bioreactor scheme, both with 80% capacity. For sterilization, CIP and SIP will be conducted after each batch. The 5,000L tank will be purchased for $55,100 and the 1,000L tank for $26,600.

15.2.2.3 Ultrafiltration/Diafiltration (PFD 02/P-66, PFD 04/P-51)

This unit is used to concentrate the protein product as well as perform a buffer exchange. The system used is a Cogent Process Scale TFF system with a 100 L tank. The filtration membrane is provided by a Pellicon 2 cassette with a 2.5 m^2 membrane area. The product is retained by the filter, while smaller particles are passed through it. Then, it washed away using the new buffer that is required to bring the pH of the solution up. Two filters will be needed for each batch for the large production bioreactor design and one filter will be needed for each batch in the small production bioreactor design. The cost of the system is $500,000 while the disposable membrane cassette is $3,600 per unit.

15.2.2.4 Storage Tank 9 (PFD 02/P-68, PFD 04/P-53)

This storage tank is used to collect the retentate from the diafiltration column. For the large production bioreactor design, it will be a 2,000L tank and for the small production bioreactor design, it will be a 500L tank, both with a maximum of 80% capacity. For sterilization, CIP and SIP will be conducted after each batch. The 2,000 L tank will be purchased for $35,900 and the 500L tank will be purchased for $22,550.

15.2.2.5 Cation Exchange Chromatography Column (PFD 02/P-70, PFD 04/P-55)

The cation exchange chromatography column is used to further purify the solution and removed impurities. The Chromaflow 1000 column will be used with the Capto S resin and both will be purchased from GE Healthcare Life Sciences. The column is made of Stainless Steel 316. The column has a bed height of 0.2m and diameter of 1.0m with a volume of 160 L. The resin has a binding capacity of

60 g mAb/L and a working linear velocity of up to 600 cm/hr. Similar to the Protein A chromatography column, the amount of mAb processed per cycle is determined by the volume of the bed and the binding capacity of the resin. For this column, 9.4 kg mAb will be processed per cycle which was determined by 60 g mAb/L*160 L. The column is operated at 25°C, at 1 bar. The cost of the column is $250,000 and the resin is $1500 per liter. For the large production bioreactor design, four cycles of cation exchange chromatography are required. For the small production bioreactor design, one cycle of cation exchange chromatography is required for each 2,000 L bioreactor.

15.2.2.6 Storage Tank 10 (PFD 02/P-72, PFD 04/P-57)

This storage tank is used to collect the effluent from the cation exchange chromatography column. For the large production bioreactor design, it will be a 2,000L tank and for the small production bioreactor design, it will be a 500L tank, both with a maximum of 80% capacity. For sterilization, CIP and SIP will be conducted after each batch. The 2,000 L tank will be purchased for $35,900 and the 500L tank will be purchased for $22,600.

15.2.3 Polishing Steps

15.2.3.1 Virus Filtration Unit (PFD 02/P-74, PFD 04/P-59)

This unit will remove the virus particles that were previously inactivated. For safety requirements, the product must contain less than one virus particle per million doses, which translates to 12-18 $\log_{10}$ clearance of endogenous retroviruses and 6 $\log_{10}$ clearance for adventitious viruses. This unit is placed at towards the end of the purification process because the risk of blockage is the lowest. The membrane used will be a Virosart HF Process Module with a 0.8 m^2 area, priced at $10,084 per filter. The Virosart CPV system targets the removal of both small non-enveloped viruses (20 nm) and larger enveloped viruses (>50 nm). Each membrane is housed in a Sartopore 2 XLG MaxiCap. Four filtration units will be used per batch for the large production bioreactor design and one unit will be used for the small production bioreactor design batch. These virus filtration units cost $10,000 each.

15.2.3.2 Hydrophobic Interaction Chromatography Column (PFD 02/P-76, PFD 04/P-61)

The hydrophobic interaction chromatography column is used as a polishing step and to remove any aggregates that may have formed due to the pH changes. The Chromaflow 1000 column from GE Healthcare Life Sciences will be used with the POROS Benzyl Ultra resin from Thermo Fisher Scientific. The column is made of Stainless Steel 316. The column has a bed height of 0.25m and diameter of 1.0m, with a volume of 200L. The resin can used with a working linear velocity of up to 600 cm/hr. The column is operated at 25°C, with a pressure of 1 bar. The cost of the column is $250,000 and the resin is $380 per liter. For the large production bioreactor, four cycles of HIC are required. For the small production bioreactor, one cycle of HIC is required for each 2,000 L bioreactor.

15.2.3.3 Storage Tank 11 (PFD 02/P-78, PFD 04/P-63)

This storage tank is used to collect the product flow through from the hydrophobic interaction chromatography column. For the large production bioreactor design, it will be a 5,000L tank and for the small production bioreactor design, it will be a 2,500L tank, both with a maximum of 80% capacity. For sterilization, CIP and SIP will be conducted after each batch.The 5,000 L tank will be purchased for $55,100 and the 2,500L tank will be purchased for $38,700.

15.2.3.4 Ultrafiltration / Diafiltration Unit (PFD 02/P-80, PFD 04/P-65)

Similar to the previous UF/DF operation, the Cogent Process Scale TFF System will be used to concentrate the product to its final titer and ensure sterility of the buffer. As before, Pellicon 2 cassettes will provide 2.5 m^2 of membrane area.

15.2.3.5 Sterile Filtration (PFD 02/P-82, PFD 04/P-67)

Sterile filtration is used as a final step and the product is filtered directly into the storage containers. This is an important step to ensure sterility before the product is frozen and stored. The filters have pore sizes of 0.2 μm and are Sartopore 2 filters from Sartorius. They can be purchased for $650 per filter.

15.2.3.6 Final Storage (PFD 02/P-84, PFD 04/P-69)

The final product from the purification process will be stored in 10L Nalgene Biotainers. These biotainers are polycarbonate and will be stored at -80°C. For the large production bioreactor design, 70 bottles will be used and 42 bottles will be used for the small production bioreactor design. The containers will be purchased for $100 from Thermo Fisher Scientific.

15.3 Additional Units

15.3.1 Pumps and Tubing

Peristaltic or diaphragm pumps will be used to transfer contents between each unit in the upstream operations. The peristaltic pump model that will be used in upstream processes is the 800 series Watson-Marlow Bredel, specifically the 825 series hygienic pump model. This model is made for shear sensitive products and has CIP and SIP in-line capability. It has a maximum operable flow rate of 33 L/min, maximum pressure of 3.5 bar, and maximum motor speed of 101 rpm. Each pump costs approximately $3,000. The two diaphragm pump models that will be used are quaternary diaphragm pumps QF150S and QF1200S from Quattroflow for bio-pharma application. These pumps have four possible flow directions, operate in the laminar flow regime with minimal shear, with maximum motor speeds of 50 Hz. The 150S model will be operated at 4 bar at varying flow rates between its minimum flow rate of 0.017 L/min and maximum flow rate of 3 L/min. The 1200S 5° Eccentric Shaft model that will be used will be operated at 3 bar at varying flow rates between its minimum flow rate of 0.17 L/min and its maximum flow rate of 20 L/min. Both the 150S and 1200S pump models are CIP and SIP sterilizable and cost $3,000 and $4,000, respectively.

In the downstream processes, only peristaltic pumps will be used. The 800 series Watson-Marlow Pump used will be the 840 model. The pump has a maximum flow rate of 8,140 L/hr, maximum pressure of 3.5 bar, and maximum motor speed of 102 rpm. Each pump costs approximately $3,000.

The tubing used between pump-heads for both upstream and downstream operations is Cole-Parmer MasterFlex BioPharm Plus Tubing. The tubing is made of platinum silicone, which provides a smooth, sterile, biocompatible surface for sensitive biopharmaceutical applications. It can be autoclaved and meets FDA standards. It can

also withstand temperatures up to 232°C, which exceeds any temperature used in this process design. The cost per foot of tubing is $49.00.

15.3.2 Heating and Cooling

All upstream units either containing cells or transferring fluids to cellular environments will be heated to 36.5°C using various methods. All WAVE bioreactor systems will be heated using electric heating with temperature sensors and control of the trays that hold the cell bags. The Xcellerex XDR bioreactor system in addition to the custom 20,000L stainless steel bioreactor will use a controlled heating jacket flowing heated sterile water at around 60°C. For all media transfer steps, the upstream process requires heating to 36.5°C before entering a bioreactor. Likewise, all cell transfer steps require that the temperature be maintained between 36 and 37°C during transfer to prevent cell death or slowed product formation. For both of these operations, the platinum silicone tubing described above in Section 15.3.1 will be jacketed with carbon-steel piping. 10% propylene glycol in U.S. Pharmacopeia (USP) grade water heated to 60°C will flow through the jacket primarily to heat culture media as it is transferred from storage tanks at 4°C to bioreactors at 36.5°C. Lastly, all media storage tanks will have a cooling jacket to cool media to 4°C. Chilled water will flow through the cooling jacket

Water-glycol solutions will be heated using a Chromalox water-glycol heater engineered from welded steel with copper sheath heating elements in itst electric heating core. The heating unit operates at a maximum temperature of 150°C and comes with electronic digital temperature process control. Water heaters (purchased from PVI Industries, LLC), cooling water units (purchased from Cole-Parmer), and water-glycol heaters (purchased from Chromalox) will already be in the plant and will be included in the annual expenses.

15.3.3 Cell Storage Tank

The engineered CHO cells will be stored in a cryogenic storage tank to maintain viability until use. The cells come in 1 mL cryogenic vials that can be stored in Thermo Scientific Nalgene cryogenic storage boxes, which can withstand temperatures below -180°C without deformation. Each box fits one hundred 1mL vials and fits into Thermolyne stainless steel, Locator 8 Cryogenic Storage Vessel. This system is built to hold liquid nitrogen with vacuum insulation, uniform temperature control, and a liquid

level monitor. Liquid nitrogen levels must be monitored precisely and replaced when the levels get too low to maintain the cells in a cryogenic state. The tank holds 60 Nalgene boxes in 90L of liquid nitrogen, which evaporates at 0.4 L/day. The costs of the storage boxes, storage vessel, and liquid nitrogen supply will be $1,700, $2,700, and 0.05$ per gallon respectively

15.3.4 Biosafety Cabinet

A biosafety cabinet will be required to provide a sterile environment to handle and transfer the vial of cells into the bag bioreactors in the inoculum prep section. The biosafety cabinet is manufactured by Thermo Scientific. The biosafety cabinet is part of the existing plant and will be included in annual expenses.

15.3.5 Product Refrigeration Unit

Until the final mAb product is shipped out of the plant for packaging and commercial sale, it must be refrigerated at -80°C. The product refrigeration units will be purchased from Thermo Scientific, sized at 33.5 cubic feet, which can hold about 900L. The units have a temperature range of -86 to -50°C. Three refrigeration units will be purchased for the Large Production Bioreactor Scheme, while two units will be purchased for the Small Production Bioreactor Scheme. The refrigerators will cost $15,100.

15.3.6 Biowaste and Neutralization Holding Tank

All biowaste produced in the process will need to be treated before disposal. All waste potentially containing live culture is sent to the biowaste tank. All other waste, such as used buffers, is sent directly to a neutralization tank. The neutralization tank will need to hold 56,700 L for the large production bioreactor scheme so four 20,000 L tanks will be used and it will need to hold 13,290 L for the small production bioreactor scheme so two 20,000L tanks will be used.

In addition, there is waste from the disposable equipment such as filters and bioreactor bags that will be handled by a waste management company. The Land Disposal Restrictions (LDR) regulations require the treatment of all hazardous pharmaceutical waste, most commonly by hazardous waste incineration, before it can be discarded in a hazardous waste landfill. [30]

15.3.7 Water for Injection Still

The WFI still is used to purify water used throughout process that needs to meet FDA guidelines. WFI is used to ensure sterility of both the product and the process equipment to help eliminate cross-contamination issues. The WFI still will already be in the plant (purchased from Telstar) and the costs will be included in the annual expenses.

15.3.8 Sterile Air Compressor and Filtration

Compressed, sterile air is required for all upstream bioreaction processes, since sparged air is the source of oxygen for the cells. An air compressor containing a medical-grade filtration unit will be purchased from Greeloy Medical. The unit requires 3200W, with a capacity of 620 L/min at 0 bar. The maximum pressure of the unit is 8 bar and the tank can process up to 120 L of air. The internal air filter only needs to be replaced once every year, but will be replaced every six months to ensure continued sterility. 10 units will be purchased for the Large Production Bioreactor Scheme, while 6 units will be purchased for the Small Production Bioreactor Scheme. These costs will be included in the annual expenses.

Further, sterile compressed air is also filtered just before entering each of the bioreactors as a quality control step. The air filters that will be inserted into the air inlet ports will be the Opticap® XL Disposable Capsule Filters with 0.22 µm Hydrophobic Durapore® Membrane purchased from Millipore Sigma. The same filters will be used to filter all of the vented gases from the bioreactors. The filters have a filtration area of 0.69 $m^2$are, are constructed from polyvinylidene fluoride (PVDF), and can be sterilized by autoclave at 126°C for 30 minutes. The filters will be replaced after each batch and cost about 400$ per filter.

15.3.9 Clean Steam Generator

The clean steam generator uses WFI to produce steam for the SIP procedures. The clean steam generator will already be in the plant, purchased from Spirax Sarco, and the costs will be included in the annual expenses. It has a maximum output of 3800 kg/hour and a maximum steam pressure of 12 bar.

15.3.10 CIP Skids

Clean-in-place (CIP) technique is used to clean equipment before the next use. The CIP Skid used in this process will be portable with a capacity to clean process tanks

up to 3 meters in diameter. The skid will include an option for steam heating to heat the cleaning solution to 85°C. The cost of CIP skids will be included in the annual expenses.

15.3.11 Buffer Transfer Containers

Buffer transfer containers are used to transfer buffer to the chromatography columns and diafiltration units. These containers will be used to mix the buffers before being used and it will be filtered before being used. CIP and SIP operations will be used to clean these containers after each batch. For the large production bioreactor design, 5,000L tanks will be used and for the small production bioreactor design, 1,000L tanks will be used.

15.3.12 Filter Integrity Test

A filter integrity test will be purchased from Millipore. This will be used to ensure that all filters are functional and do not have any tears or blockages prior to each batch. This is important in minimizing loss from manufacturing error and will be included in the annual expenses.

15.3.13 Water Treatment Package

Although WFI will be used for most of the water requirements in the process, U.S. Pharmacopeia (USP) grade water is needed for temperature control needs in the bioreactor process. This water will not be in contact with the cell culture, but it will inserted into the stainless steel bioreactor jackets for heating and cooling purposes. The cost for the water treatment package (MECO's MASTERpak™ LT) is included in the annual expenses.

15.3.14 Biowaste Inactivation System

The biowaste inactivation system is needed to kill any live cells remaining in the bio-waste tank. This includes liquid volumes from all CIP and SIP washes from the main bioreactors and primary recovery. The biowaste inactivation system is part of the existing plant.

15.3.15 Waste Neutralization System

The waste neutralization system is used to adjust the pH of liquid waste, which contains no cells, to 7.0. The waste can be disposed directly into the sewer line. The waste neutralization system is part of the existing plant and will be included in the annual expenses.

15.3.16 Quality Control Lab

A quality control lab will be used to ensure the manufactured product meets the quality specifications and FDA regulations. Various samples will be taken throughout the process, including all upstream bioreactors, and downstream virus inactivation and virus filtration units. This lab is part of the existing plant and will be included in the annual expenses

16. Specification Sheets

Blending Tank (PFD 01/P-1)

Description and Function: This blending tank will mix cell culture media powder with WFI.

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Dry Media	1.19	0
Water	49.7	0
NaOH	0.065	0
$NaHCO_3$	0.140	0
Wet Media	0	50.0

Characteristics

Volume:	75 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Blending Tank:	$12,500

Dead-End Filter (PFD 01/P-3)

Description and Function	The 0.2 µm dead-end filter is used to remove larger contaminants from blended culture media. The filter capsules and housing are disposable and ready-to-use.		
Vendor	Millipore Sigma		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Wet Media	50.0	50.0
Characteristics	Model:	Opticap XLT10, Sterile	
	Filtration Area:	0.57 m^2	
	Throughput:	2,000 $L/m^2/h$	
	Max. Differential Pressure:	6.9 bar at 25°C	
	Sterilization:	Disposable	
Operation Conditions	Temperature:	25°C	
	Pressure:	0.5 bar	
Purchase Cost	Filter Membrane & Housing:	$400	

Storage Tank (PFD 01/P-21)

Description and Function: The storage tank holds blended and filtered cell culture media at 4°C until further use.

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Wet Media	50.0	0.00

Characteristics

Volume:	75 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	4°C
Pressure:	2 bar

Purchase Cost

Storage Tank:	$12,500

250 mL Shaker Flask (PFD 01/P-7)

Description and Function

The 250 mL Shaker Flask is used for cell growth in first inoculum preparation step after cryogenic recovery of the CHO cells. The Shaker Flask is placed on a low speed orbital shaker and the combined apparatus is incubated in a CO_2 Incubator.

Vendor

Corning (Flask & Orbital Shaker)
Thermo Fisher Scientific (Incubator)

Operation

Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells:	0.00000471	0.0000166
Wet Media	0.030	0.125
Product	0.00	0.00

Characteristics

Model:	Corning 4444-250
Flask Capacity:	250 mL
Working Capacity:	80%
Material:	Pyrex
Packaging:	6 pc
Sterilization:	Autoclave, 121°C, 60 minutes
Model:	Corning LSE 6780-FP
Speed:	60 rpm
Frequency Range:	50/60 Hz
Tray Size:	30 cm x 30 cm
Base Size:	25.5 cm x 32.0 cm x 16.0 cm
Model:	Thermo Scientific Forma Series 3
Interior Material:	Stainless Steel 304
Dimensions (LxWxH):	54.1 cm x 68.1 cm x 50.8 cm

Operation Conditions

Temperature:	36.5°C
Pressure:	1 bar
pH:	7.1
dO_2:	40%
Duration:	3 days

Purchase Cost

Shaker Flask:	$160
Orbital Shaker:	$900
Incubator:	$7,900

25 L Single-Use Bioreactor (PFD 01/P-9)

Description and Function	The 25L WAVE Bioreactor is used for cell growth in second inoculum preparation step. The single-use system is equipped with a rocker, gas mixers, pumps, and cell bags. The bags are disposable and pre-sterilized. The system also offers high level sensors and automated control for temperature, liquid transfer, dissolved oxygen, and pH.		
Vendor	GE Healthcare and Life Sciences		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Cells	0.0000166	0.0000586
	Wet Media	0.125	12.5
	Product	0.00	0.00
Characteristics	Model:	ReadyToProcess WAVE 25	
	Rocker Dimensions:	404 mm x 205 mm x 560 mm	
	Tray 50 Dimensions:	800 mm x 70 mm x 610 mm	
	Lid 50 Dimensions:	800 mm x 260 mm x 610 mm	
	CBCU Dimensions:	276 mm x 115 mm x 280 mm	
	Frequency:	50/60 Hz	
	Bag Size:	22 L	
	Sterilization:	Plastic, Disposable	
Operation Conditions	Temperature:	36.5°C	
	Pressure:	2 bar	
	pH:	7.1	
	dO_2:	40%	
	Agitation Speed:	15 rpm	
	Rocking Angle:	7°	
	Duration:	3 days	
Purchase Cost	Bioreactor with control:	$60,000	
	CBCU gas mixer:	$1,000	
	Disposable Cellbag:	$500	

Diaphragm Pumps (PFD 01/P-16,22,[38/39])

Description and Function	The pumps are used to transfer media and cells for upstream bioreaction steps. The pumps are sterile and designed for shear-sensitive biopharmaceutical applications. The diaphragm pumps have 4 inlet and 4 outlets per pump	
Vendor	QuattroFlow	
Operation	Batch	
Characteristics	Model:	150 S
	Pumphead Material:	Stainless Steel 316 L
	Minimum Flow Rate:	0.01 L/min
	Maximum Flow Rate:	3.00 L/min
	Maximum Pressure:	6 bar
	Sterilization:	CIP, SIP
Operation Conditions	Pressure:	4 bar
	Flow Rate:	Variable (0.01-33 L/min)
Purchase Cost	Pump:	$3,000

Diaphragm Pumps (PFD 01/P-28,[30/31])

Description and Function	The pumps are used to transfer media and cells for upstream bioreaction steps. The pumps are sterile and designed for shear-sensitive biopharmaceutical applications. The diaphragm pumps have 4 inlet and 4 outlets per pump	
Vendor	QuattroFlow	
Operation	Batch	
Characteristics	Model:	1200 S
	Pumphead Material:	Stainless Steel 316 L
	Minimum Flow Rate:	0.33 L/min
	Maximum Flow Rate:	20 L/min
	Maximum Pressure:	6 bar
	Sterilization:	CIP, SIP
Operation Conditions	Pressure:	3 bar
	Flow Rate:	Variable (0.33-20 L/min)
Purchase Cost	Pump:	$4,000

100 L Single-Use Bioreactor (PFD 01/P-29)

Description and Function

The 100L WAVE Bioreactor is used for cell growth in cell seeding. The single-use system is equipped with a rocker base unit with internal gas pumps and cell bags. The bags are disposable and pre-sterilized. The system also offers high level sensors and automated control for temperature, liquid transfer, dissolved oxygen, and pH.

Vendor

GE Healthcare and Life Sciences

Operation

Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0.0000586	0.000308
Wet Media	12.5	50.0
Product	0.00	0.00

Characteristics

Model:	WAVE Bioreactor 200
Dimensions:	1.85 m x 1.10 m x 1.12 m
Frequency:	50/60 Hz
Bag Size:	100 L
Sterilization:	Plastic, Disposable

Operation Conditions

Temperature:	36.5°C
Pressure:	2 bar
pH:	7.1
dO_2:	40%
Agitation Speed:	25 rpm
Rocking Angle:	8°
Duration:	3 days

Purchase Cost

Bioreactor w control:	$90,000
Disposable Cellbag:	$800

Blending Tank (PFD 01/P-11)

Description and Function: This blending tank will mix cell culture media powder with WFI.

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Dry Media	67.1	0.00
Water	2980	0.00
NaOH	3.90	0.00
$NaHCO_3$	8.40	0.00
Wet Media	0.00	3000

Characteristics

Volume:	4,000 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Blending Tank:	$51,000

Blending Tank (PFD 01/P-17)

Description and Function: This blending tank will mix feed supplement CellBoost 7a media powder with WFI.

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Dry Media	978	0.00
Water	5370	0.00
NaOH	7.54	0.00
Wet Media	0.00	5400

Characteristics

Volume:	7,000 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Blending Tank:	$63,200

Blending Tank (PFD 01/P-23)

Description and Function: This blending tank will mix feed supplement CellBoost 7b media powder with WFI.

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Dry Media	51.1	0.00
Water	537	0.00
NaOH	0.754	0.00
Wet Media	0.00	540

Characteristics

Volume:	700 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Blending Tank:	$24,300

Dead-End Filter (PFD 01/P-13)

Description and Function	The 0.2 µm dead-end filter is used to remove larger contaminants from blended culture media. The filter capsules and housing are disposable and ready-to-use.		
Vendor	Millipore Sigma		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Wet Media	3000	3000
Characteristics	Model:	Opticap XLT10, Sterile	
	Filtration Area:	0.57 m^2	
	Throughput:	2,000 $L/m^2/h$	
	Max. Differential Pressure:	6.9 bar at 25°C	
	Sterilization:	Disposable	
Operation Conditions	Temperature:	25°C	
	Pressure:	0.5 bar	
Purchase Cost	Filter Membrane & Housing:	$400	

Dead-End Filter (PFD 01/P-19)

Description and Function	The 0.2 µm dead-end filter is used to remove larger contaminants from blended feed supplement 7a media. The filter capsules and housing are disposable and ready-to-use.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Wet Media	5400	5400
Characteristics	Model:	Opticap XLT10, Sterile	
	Filtration Area:	0.57 m^2	
	Throughput:	2,000 $L/m^2/h$	
	Max. Differential Pressure:	6.9 bar at 25°C	
	Sterilization:	Disposable	
Operation Conditions	Temperature:	25°C	
	Pressure:	0.5 bar	
Purchase Cost	Filter Membrane & Housing:	$400	

Dead-End Filer (PFD 01/P-25)

Description and Function	The 0.2 µm dead-end filter is used to remove larger contaminants from blended culture media. The filter capsules and housing are disposable and ready-to-use.		
Vendor	Millipore Sigma		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Wet Media	540	540
Characteristics	Model:	Opticap XLT10, Sterile	
	Filtration Area:	0.57 m^2	
	Throughput:	2,000 $L/m^2/h$	
	Max. Differential Pressure:	6.9 bar at 25°C	
	Sterilization:	Disposable	
Operation Conditions	Temperature:	25°C	
	Pressure:	0.5 bar	
Purchase Cost	Filter Membrane & Housing:	$400	

Storage Tank (PFD 01/P-15)

Description and Function	The storage tank holds blended and filtered cell culture media at 4°C until further use.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Wet Media	3000	0.00
Characteristics	Volume:	4,000 L	
	Working Capacity:	80%	
	Material:	Stainless Steel 316	
	Height/Diameter Ratio:	2/1	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	4°C	
	Pressure:	2 bar	
Purchase Cost	Storage Tank:	$51,000	

Storage Tank (PFD 01/P-21)

Description and Function	The storage tank holds blended and filtered cell culture media at 4°C until further use.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Wet Media	200	0.00
Characteristics	Volume:	250 L	
	Working Capacity:	80%	
	Material:	Stainless Steel 316	
	Height/Diameter Ratio:	2/1	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	4°C	
	Pressure:	2 bar	
Purchase Cost	Storage Tank:	$18,000	

Storage Tank (PFD 01/P-27)

Description and Function: The storage tank holds blended and filtered cell culture media at 4°C until further use.

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Wet Media	20.0	0.00

Characteristics

Volume:	25 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	4°C
Pressure:	2 bar

Purchase Cost

Storage Tank:	$9,200

500 L Single-Use Seed Bioreactors (PFD 01/P-32,33)

Description and Function

The 500L WAVE Bioreactor is used for cell growth in cell seeding. The single-use system is equipped with a rocker base unit with internal gas pumps and cell bags. The bags are disposable and pre-sterilized. The system also offers high level sensors and automated control for temperature, liquid transfer, dissolved oxygen, and pH. Two of these bioreactors operate in parallel.

Vendor

GE Healthcare and Life Sciences

Operation

Batch

Materials Handled

	Input (kg/batch)	**Output (kg/batch)**
Cells	0.000308	0.000813
Wet Media	25.0	250
Product	0.00	0.00

Characteristics

Model:	WAVE Bioractor 500/1000 system
Dimensions:	2.26 m x 1.24 m x 1.60 m
Frequency:	50/60 Hz
Bag Size:	500 L
Sterilization:	Plastic, Disposable

Operation Conditions

Temperature:	36.5°C
Pressure:	2 bar
pH:	7.1
dO_2:	40%
Agitation Speed:	15 rpm
Rocking Angle:	4°
Duration:	3 days

Purchase Cost

Bioreactor with control:	$150,000
Disposable Cellbag:	$1,000

2,000 L Single-Use Seed Bioreactors (PFD 01/P-36,37)

Description and Function: The 2000L Xcellerex XDR Bioreactor is used for cell growth in cell seeding. The single-use system is equipped with a jacketed bioreactor vessel, gas mixing cabinet, control console, and cell bags. The bags are disposable and pre-sterilized. The system also offers high level sensors and automated control for temperature, liquid transfer, dissolved oxygen, and pH. Two of these bioreactors operate in parallel.

Vendor: GE Healthcare and Life Sciences

Operation: Batch

Materials Handled

	Input (kg/batch)	**Output (kg/batch)**Cells
	0.00429	0.000813
Wet Media	250	1600
Product	0.00	0.00

Characteristics

Model:	Xcellerex XDR-2000 system
Height/Diameter Ratio:	1.5/1
Impeller Type, Angle:	4 blades, 40° pitch
Impeller/Bag Diameter Ratio:	0.34
Bag Size:	2000 L
Sterilization:	Plastic, Disposable

Operation Conditions

Temperature:	36.5°C
Pressure:	2 bar
pH:	7.1
dO_2:	40%
Agitation Speed:	110 rpm
Duration:	3 days

Purchase Cost

Bioreactor with control:	$250,000
Disposable Cellbag:	$2,500

Blending Tank (PFD 01/P-46)

Description and Function: This blending tank will mix cell culture media powder with WFI.

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Dry Media	107	0.00
Water	4470	0.00
NaOH	5.85	0.00
$NaHCO_3$	12.6	0.00
Wet Media	0.00	4500

Characteristics

Volume:	6,000 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Blending Tank:	$59,400

Dead-End Filter (PFD 01/P-48)

Description and Function	The 0.2 µm dead-end filter is used to remove larger contaminants from blended culture media. The filter capsules and housing are disposable and ready-to-use.		
Vendor	Millipore Sigma		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Wet Media	4500	4500
Characteristics	Model:	Opticap XLT10, Sterile	
	Filtration Area:	0.57 m^2	
	Throughput:	2,000 $L/m^2/h$	
	Max. Differential Pressure:	6.9 bar at 25°C	
	Sterilization:	Disposable	
Operation Conditions	Temperature:	25°C	
	Pressure:	0.5 bar	
Purchase Cost	Filter Membrane & Housing:	$400	

Storage Tank (PFD 01/P-50)

Description and Function	The storage tank holds blended and filtered cell culture media at 4°C until further use.	
Operation	Batch	
Materials Handled	**Input (kg/batch)**	**Output (kg/batch)**
	Wet Media 4500	0.00
Characteristics	Volume:	6,000 L
	Working Capacity:	80%
	Material:	Stainless Steel 316
	Height/Diameter Ratio:	2/1
	Sterilization:	CIP/SIP
Operation Conditions	Temperature:	4°C
	Pressure:	2 bar
Purchase Cost	Storage Tank:	$59,400

Storage Tank (PFD 01/P-41)

Description and Function

The storage tank holds blended and filtered cell culture media at 4°C until further use.

Operation

Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Wet Media	5200	0.00

Characteristics

Volume:	7,500 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	4°C
Pressure:	2 bar

Purchase Cost

Storage Tank:	$69,400

Storage Tank (PFD 01/P-44)

Description and Function

The storage tank holds blended and filtered cell culture media at 4°C until further use.

Operation

Batch

Materials Handled

	Input (kg/batch)	**Output (kg/batch)**
Wet Media	520	0.00

Characteristics

Volume:	750 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	4°C
Pressure:	2 bar

Purchase Cost

Storage Tank:	$25,500

20,000 L Stainless Steel Production Bioreactor (PFD 01/P-16)

Description and Function: The 20,000L Bioreactor is used for cell growth to peak density followed by maximum product formation. The system is equipped with a heating jacket, mixing and sparging units, and PID control for temperature, liquid transfer, dissolved oxygen, dissolved carbon dioxide and pH.

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0.00429	63.6
Wet Media	3200	13500
Product	0.00	40.1

Characteristics

Volume:	20,000 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Impeller/Tank Diameter Ratio:	1/3
Blade Height/Impeller Diameter:	1/5
Blade Width/Impeller Diameter:	1/4
Number of Blades, Pitch:	4, 40°
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	36.5°C
Pressure:	2 bar
pH:	7.1
dO_2:	40%
Agitation Power:	0.055 W/kg
Air Sparging Rate:	0.0194 vvm
Duration:	19 days

Purchase Cost

Total Bioreactor:	$1,500,000

Peristaltic Pumps (PFD 01/P-2,4,6,8,10,12,14,18,20,24,26,34,35,40,42,43,45,47,49,50,53)

Description and Function	The pumps are used to transfer media and cells for upstream bioreaction steps. The pumps are sterile and designed for shear-sensitive biopharmaceutical applications.	
Vendor	Watson-Marlow	
Operation	Batch	
Characteristics	Model:	825 series
	Pumphead Material:	Aluminum alloy
	Support and Frame Material:	Stainless steel 304
	Maximum Flow Rate:	33 L/min
	Maximum Pressure:	3.5 bar
	Sterilization:	CIP, SIP
Operation Conditions	Pressure:	3 bar
	Flow Rate:	Variable (0.1-33 L/min)
Purchase Cost	Pump:	$3,000

Centrifuge (PFD 02/P-54)

Description and Function	This centrifuge will separate the cells from the cell culture liquid that has the solubilized monoclonal antibody product.		
Vendor	GEA		
Operation	Continuous		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Cells	75.4	0
	Media	0	0
	Water	13500	13500
	Product	40.1	38.5
Characteristics	Model:	CSE 170	
	Centrifuge Type:	Disc Stack Centrifuge	
	Material:	Stainless Steel 316	
	Capacity Range:	3000-6000 L/h	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	25°C	
	Throughput:	3375 L/h	
Purchase Cost	Centrifuge:	$1,500,000	

Storage Tank 6 (PFD 02/P-56)

Description and Function	This storage tank will collect the liquid product from the centrifuge.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Cells	0	0
	Media	0	0
	Water	13500	13500
	Product	38.5	38.5
Characteristics	Material:	Stainless Steel 316 L	
	Volume:	20,000L	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	25°C	
	Pressure:	1 bar	
Purchase Cost	Centrifuge:	$104,700	

Depth Microfiltration Unit (PFD02/P-58)

Description and Function: The depth filter is used to remove larger particles not removed from centrifugation. It has two distinct layers with different pore sizes (0.1-1μm) to avoid plugging and increase filter capacity.

Vendor: Millipore Sigma

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Water	13500	13500
Product	38.5	37.3

Characteristics

Model:	Millistak Pod Filter
Filter:	X0HC
Protein Throughput:	21 L/min/m^2
Max. Differential Pressure:	2.1 bar
Max. Operating Pressure:	3.5 bar
Filter effective area:	1.1 m^2
Unit Sterilization:	SIP
Filter Sterilization:	Disposable

Operation Conditions

Temperature:	25°C
Operating Pressure:	1 bar

Purchase Cost

Filter Housing:	$67,300
Filter:	$750 each

Storage Tank 7 (PFD 02/P-60)

Description and Function	This storage tank will collect the filtrate liquid from the depth filtration unit.		
Operation	Batch		
Materials Handled		Input (kg/batch)	Output (kg/batch)
	Cells	0	0
	Media	0	0
	Water	13500	13500
	Product	37.3	37.3
Characteristics	Material:	Stainless Steel 316	
	Volume:	20,000L	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	25°C	
	Pressure:	1 bar	
Purchase Cost	Tank:	$104,700	

Protein A Chromatography Column (PFD 02/P-62)

Description and Function: The Protein A Chromatography column uses a resin that selectively binds the monoclonal antibody product. This step is the first isolation step in the purification process and is useful in eliminating host cell proteins, DNA, cell culture media components.

Vendor: GE Healthcare Life Sciences

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Centrifuge effluent	13500	0
Equilibration buffer	6800	0
Wash buffer	800	0
Elution buffer	3200	3200
Regeneration buffer	2400	0
CIP buffer	3200	0
Protein A waste	0	26700
Product	37.3	34.4

Characteristics

Model:	Chromaflow 1000/100-300
Column Diameter:	1.0 m
Bed Height:	0.25 m
Material of Construction:	Stainless Steel 316 L
Bed Volume:	200 L
Resin:	MabSelect Sure LX
Binding Capacity:	50 g mAB/L resin
Working Linear Velocity:	250-400 cm/hr
pH Stability:	3-12
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Column:	$250,000
Resin:	$8,000/liter

Storage Tank 8 (PFD 02/P-64)

Description and Function	This storage tank will collect the eluent from the Protein A Chromatography column.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Cells	0	0
	Media	0	0
	Water	3200	3200
	Product	34.4	34.4
Characteristics	Material:	Stainless Steel 316	
	Volume:	5,000L	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	25°C	
	Pressure:	1 bar	
Purchase Cost	Tank:	$55,100	

Ultrafiltration/Diafiltration Unit (PFD 02/P-66)

Description and Function: This unit is used for buffer exchange to raise the pH of the solution and concentrate it by 5 times. It is done using tangential flow filtration.

Vendor: Millipore Sigma

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Water	3200	640
Product	34.4	33.3

Characteristics

Model:	Cogent® TFF System
Protein Throughput:	21 L/min/m^2
Max. Operating Pressure:	6.8 bar
Filter effective area:	1.1 m^2
Unit Sterilization:	SIP
Filter Sterilization:	Disposable

Operation Conditions: Temperature: 25°C

Purchase Cost

Unit:	$500,000
Filter:	$3600/filter

Storage Tank 9 (PFD 02/P-68)

Description and Function	This storage tank will collect the retentate from the diafiltration operation.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Cells	0	0
	Media	0	0
	Water	640	640
	Product	33.3	33.3
Characteristics	Material:	Stainless Steel 316	
	Volume:	2,000L	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	25°C	
	Pressure:	1 bar	
Purchase Cost	Tank:	$35,900	

Cation Exchange Chromatography Column (PFD 02/P-70)

Description and Function: The cation exchange chromatography column binds positively charged proteins and is used eliminate DNA, some host cell proteins, and leached Protein A.

Vendor: GE Healthcare Life Sciences

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Diafiltration effluent	640	0
Equilibration buffer	3200	0
Wash buffer	3200	0
Elution buffer	1290	1290
Regeneration buffer	1280	0
CIP buffer	1920	0
Cation exchange waste	0	10240
Product	33.3	30.7

Characteristics

Model:	Chromaflow 1000/100-300
Column Diameter:	1.0 m
Bed Height:	0.2 m
Material of Construction:	Stainless Steel 316 L
Bed Volume:	160 L
Resin:	Capto S
Binding Capacity:	60 g mAB/L resin
Working Linear Velocity:	200-600 cm/hr
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Filter Housing:	$250,000
Filter:	$1,500/L

Storage Tank 10 (PFD 02/P-72)

Description and Function	This storage tank will collect the eluent from the Cation Exchange Chromatography.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Cells	0	0
	Media	0	0
	Water	1290	1290
	Product	30.7	30.7
Characteristics	Material:	Stainless Steel 316	
	Volume:	2,000L	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	25°C	
	Pressure:	1 bar	
Purchase Cost	Tank:	$35,900	

Virus Filtration Unit (PFD 02/P-74)

Description and Function	The virus filtration unit is used to remove viruses using size based membrane separation.		
Vendor	Sartorius		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Cells	0	0
	Media	0	0
	Water	1290	1290
	Product	30.7	29.1
Characteristics	Model:	Virosart® CPV	
	Filter effective area:	1.8 m^2	
	Sterilization:	SIP	
	Membrane:	Disposable	
Operation Conditions	Temperature:	25°C	
Purchase Cost	Filter:	$10,100/filter	

Hydrophobic Interaction Chromatography Column (PFD 02/P-76)

Description and Function: The hydrophobic interaction chromatography column is run in flow through mode and removes product and process-related impurities, such as aggregates.

Vendor: Column: GE Healthcare and Life Sciences
Resin: Thermo Fisher Scientific

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Filtrate	1290	1290
Equilibration buffer	4000	0
Wash buffer	2210	2210
Elution buffer	4000	0
Regeneration buffer	2400	0
CIP buffer	4000	0
Cation exchange waste	0	14400
Product	29.1	26.8

Characteristics

Model:	Chromaflow 1000/100-300
Column Diameter:	1.0 m
Bed Height:	0.25 m
Material of Construction:	Stainless Steel 316 L
Bed Volume:	200 L
Resin:	POROS Benzyl Ultra
Working Linear Velocity:	200-500 cm/hr
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Column:	$250,000
Resin:	$3,800/10 L

Storage Tank 11 (PFD 02/P-78)

Description and Function	This storage tank will collect the product stream from the hydrophobic interaction chromatography.		
Operation	Batch		
Materials Handled		Input (kg/batch)	Output (kg/batch)
	Cells	0	0
	Media	0	0
	Water	3500	3500
	Product	26.8	26.8
Characteristics	Material:	Stainless Steel 316	
	Volume:	5,000L	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	25°C	
	Pressure:	1 bar	
Purchase Cost	Tank:	$55,100	

Ultrafiltration/Diafiltration Unit (PFD 02/P-80)

Description and Function: The diafiltration unit is used for buffer exchange for the final solution that the product will be stored in PBS. The ultrafiltration is used to concentrate the solution by 5 times.

Vendor: Millipore Sigma

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Water	3500	700
Product	26.8	26.0

Characteristics

Model:	Cogent® TFF System
Protein Throughput:	21 L/min/m^2
Max. Operating Pressure:	6.8 bar
Filter effective area:	1.1 m^2
Unit Sterilization:	SIP
Filter Sterilization:	Disposable

Operation Conditions: Temperature: 25°C

Purchase Cost

Unit:	$500,000
Filter:	$3600/filter

Sterile Filtration Unit (PFD 02/P-82)

Description and Function: The sterile filters are 0.2 μm filters that are used as the final purification step. It is used to create a sterile product before it is frozen and then sent to formulation.

Vendor: Sarotorius

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Water	700	700
Product	26.0	25.2

Characteristics

Model:	Sartopore 2 0.2μm
Membrane Filter Material:	Polyethersulfone (PES)
Max. Differential Pressure:	5 bar at 20°C
Filtration Area:	1.8 m^2
Unit Sterilization:	SIP
Filter Sterilization:	Disposable

Operation Conditions

Temperature:	25°C
Operating Pressure:	1 bar

Purchase Cost

Filter:	$650/filter

Final Storage (PFD 02/P-84)

Description and Function: The purified product will be stored in 10L containers and stored at -80°C.

Vendor: Thermo Fisher Scientific

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Water	700	700
Product	25.2	25.2

Characteristics

Volume:	10 L
Material:	Polycarbonate
Sterilization:	Disposable

Operation Conditions

Temperature:	25°C
Operating Pressure:	1 bar

Purchase Cost

Filter:	$100/container

Pumps (PFD 02/P-55, P-57, P-59, P-61, P-63, P-65, P-67, P-69, P-71, P-73, P-75, P-77, P-79, P-81)

Description and Function	The pumps are used to transfer liquid. These are high-flow hygienic pumps that are designed for low-shear sanitary pumping. They are ideal for viscous or shear sensitive products.	
Vendor	Watson-Marlow	
Operation	Batch	
Characteristics	Model:	840 Peristaltic Pump
	Pumphead Material:	Aluminum Alloy
	Flow Rate:	65-8140 L/hr
	Max Pressure:	3.5 bar
	Sterilization:	CIP/SIP
Operation Conditions	Temperature:	25°C
	Power:	0.55-3 kW
Purchase Cost	Pump:	$3000

Blending Tank (PFD 03/P-1)

Description and Function: This blending tank will mix cell culture media powder with WFI.

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Dry Media	5.14	0.00
Water	229	0.00
NaOH	0.299	0.00
$NaHCO_3$	0.644	0.00
Wet Media	0.00	230

Characteristics

Volume:	300 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Blending Tank:	$18,100

Dead-End Filter (PFD 03/P-3)

Description and Function	The 0.2 µm dead-end filter is used to remove larger contaminants from blended culture media. The filter capsules and housing are disposable and ready-to-use.
Vendor	Millipore Sigma
Operation	Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Wet Media	230	230

Characteristics

Model:	Opticap XLT10, Sterile
Filtration Area:	0.57 m^2
Throughput:	2,000 $L/m^2/h$
Max. Differential Pressure:	6.9 bar at 25°C
Sterilization:	Disposable

Operation Conditions

Temperature:	25°C
Operating Pressure:	0.5 bar

Purchase Cost: Filter Membrane and Housing: $400

Storage Tank (PFD 03/P-5)

Description and Function: The storage tank holds blended and filtered cell culture media at 4°C until further use.

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Wet Media	230	230

Characteristics

Volume:	300 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	4°C
Pressure:	2 bar

Purchase Cost

Storage Tank:	$18,100

250 mL Shaker Flask (PFD 03/P-7)

Description and Function

The 250 mL Shaker Flask is used for cell growth in first inoculum preparation step after cryogenic recovery of the CHO cells. The Shaker Flask is placed on a low speed orbital shaker and the combined apparatus is incubated in a CO_2 Incubator.

Vendor

Corning (Flask & Orbital Shaker)
Thermo Fisher Scientific (Incubator)

Operation

Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells:	0.00000471	0.0000166
Wet Media	0.030	0.125
Product	0.00	0.00

Characteristics

Model:	Corning 4444-250
Flask Capacity:	250 mL
Working Capacity:	80%
Material:	Pyrex
Packaging:	6 pc
Sterilization:	Autoclave, 121°C, 60 minutes
Model:	Corning LSE 6780-FP
Speed:	60 rpm
Frequency Range:	50/60 Hz
Tray Size:	30 cm x 30 cm
Base Size:	25.5 cm x 32.0 cm x 16.0 cm
Model:	Thermo Scientific Forma Series 3
Interior Material:	Stainless Steel 304
Dimensions (LxWxH):	54.1 cm x 68.1 cm x 50.8 cm

Operation Conditions

Temperature:	36.5°C
Pressure:	1 bar
pH:	7.1
dO_2:	40%
Duration:	3 days

Purchase Cost

Shaker Flask:	$160
Orbital Shaker:	$900
Incubator:	$7,900

25 L Single-Use Bioreactor (PFD 03/P-9)

Description and Function: The 25L WAVE Bioreactor is used for cell growth in second inoculum preparation step. The single-use system is equipped with a rocker, gas mixers, pumps, and cell bags. The bags are disposable and pre-sterilized. The system also offers high level sensors and automated control for temperature, liquid transfer, dissolved oxygen, and pH.

Vendor: GE Healthcare and Life Sciences

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0.0000166	0.0000586
Wet Media	0.125	12.5
Product	0.00	0.00

Characteristics

Model:	ReadyToProcess WAVE 25
Rocker Dimensions:	404 mm x 205 mm x 560 mm
Tray 50 Dimensions:	800 mm x 70 mm x 610 mm
Lid 50 Dimensions:	800 mm x 260 mm x 610 mm
CBCU Dimensions:	276 mm x 115 mm x 280 mm
Bag Size:	22 L
Sterilization:	Plastic, Disposable

Operation Conditions

Temperature:	36.5°C
Pressure:	2 bar
pH:	7.1
dO_2:	40%
Agitation Speed:	15 rpm
Rocking Angle:	7°
Duration:	3 days

Purchase Cost

Bioreactor:	$60,000
CBCU gas mixer:	$1,000
Disposable Cellbag:	$500

500 L Single-Use Seed Bioreactors (PFD 03/P-23)

Description and Function: The 500L WAVE Bioreactor is used for cell growth in cell seeding. The single-use system is equipped with a rocker base unit with internal gas pumps and cell bags. The bags are disposable and pre-sterilized. The system also offers high level sensors and automated control for temperature, liquid transfer, dissolved oxygen, and pH.

Vendor: GE Healthcare and Life Sciences

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0.0000586	0.00162
Wet Media	25.0	250
Product	0.00	0.00

Characteristics

Model:	WAVE Bioractor 500/1000 system
Dimensions:	2.26 m x 1.24 m x 1.60 m
Frequency:	50/60 Hz
Bag Size:	500 L
Sterilization:	Plastic, Disposable

Operation Conditions

Temperature:	36.5°C
Pressure:	2 bar
pH:	7.1
dO_2:	40%
Agitation Speed:	15 rpm
Rocking Angle:	4°
Duration:	6 days

Purchase Cost

Bioreactor with control:	$150,000
Disposable Cellbag:	$1,000

Blending Tank (PFD 03/P-11)

Description and Function: This blending tank will mix feed supplement CellBoost 7a media powder with WFI.

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Dry Media	126	0.00
Water	690	0.00
NaOH	0.904	0.00
Wet Media	0.00	695

Characteristics

Volume:	900 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Blending Tank:	$26,000

Blending Tank (PFD 03/P-17)

Description and Function	This blending tank will mix feed supplement CellBoost 7b media powder with WFI.		
Operation	Batch		
Materials Handled		Input (kg/batch)	Output (kg/batch)
	Dry Media	6.62	0.00
	Water	69.5	0.00
	NaOH	0.0910	0.00
	Wet Media	0.00	70.0
Characteristics	Volume:	90 L	
	Working Capacity:	80%	
	Material:	Stainless Steel 316	
	Height/Diameter Ratio:	2/1	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	25°C	
	Pressure:	1 bar	
Purchase Cost	Blending Tank:	$12,700	

Dead-End Filter (PFD 03/P-13)

Description and Function: The 0.2 µm dead-end filter is used to remove larger contaminants from blended feed supplement 7a media. The filter capsules and housing are disposable and ready-to-use.

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Wet Media	695	695

Characteristics

Model:	Opticap XLT10, Sterile
Filtration Area:	0.57 m^2
Throughput:	2,000 $L/m^2/h$
Max. Differential Pressure:	6.9 bar at 25°C
Sterilization:	Disposable

Operation Conditions

Temperature:	25°C
Pressure:	0.5 bar

Purchase Cost: Filter Membrane & Housing: $400

Dead-End Filter (PFD 03/P-19)

Description and Function	The 0.2 µm dead-end filter is used to remove larger contaminants from blended culture media. The filter capsules and housing are disposable and ready-to-use.		
Vendor	Millipore Sigma		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Wet Media	70.0	70.0
Characteristics	Model:	Opticap XLT10, Sterile	
	Filtration Area:	0.57 m^2	
	Throughput:	2,000 $L/m^2/h$	
	Max. Differential Pressure:	6.9 bar at 25°C	
	Sterilization:	Disposable	
Operation Conditions	Temperature:	25°C	
	Pressure:	0.5 bar	
Purchase Cost	Filter Membrane & Housing:	$400	

Storage Tank (PFD 03/P-15)

Description and Function	The storage tank holds blended and filtered cell culture media at 4°C until further use.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Wet Media	45.0	0.00
Characteristics	Volume:	50 L	
	Working Capacity:	80%	
	Material:	Stainless Steel 316	
	Height/Diameter Ratio:	2/1	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	4°C	
	Pressure:	2 bar	
Purchase Cost	Storage Tank:	$10,700	

Storage Tank (PFD 03/P-21)

Description and Function	The storage tank holds blended and filtered cell culture media at 4°C until further use.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Wet Media	5.00	0.00
Characteristics	Volume:	25 L	
	Working Capacity:	80%	
	Material:	Stainless Steel 316	
	Height/Diameter Ratio:	2/1	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	4°C	
	Pressure:	2 bar	
Purchase Cost	Storage Tank:	$9,100	

Blending Tank (PFD 03/P-31)

Description and Function

This blending tank will mix cell culture media powder with WFI.

Operation

Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Dry Media	19.7	0.00
Water	874	0.00
NaOH	1.44	0.00.
$NaHCO_3$	3.11	000
Wet Media	0.00	880

Characteristics

Volume:	1,100 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Blending Tank:	$28,200

Dead-End Filter (PFD 03/P-33)

Description and Function

The 0.2 µm dead-end filter is used to remove larger contaminants from blended culture media. The filter capsules and housing are disposable and ready-to-use.

Operation

Millipore Sigma

Materials Handled

Batch

	Input (kg/batch)	Output (kg/batch)
Wet Media	880	880

Characteristics

Model:	Opticap XLT10, Sterile
Filtration Area:	0.57 m^2
Throughput:	2,000 $L/m^2/h$
Max. Differential Pressure:	6.9 bar at 25°C
Sterilization:	Disposable

Operation Conditions

Temperature:	25°C
Pressure:	0.5 bar

Purchase Cost

Filter Membrane & Housing: $400

Storage Tank (PFD 03/P-35)

Description and Function	The storage tank holds blended and filtered cell culture media at 4°C until further use.
Operation	Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Wet Media	880	0.00

Characteristics

Volume:	1,100 L
Working Capacity:	80%
Material:	Stainless Steel 316
Height/Diameter Ratio:	2/1
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	4°C
Pressure:	2 bar

Purchase Cost

Storage Tank:	$28,200

Storage Tank (PFD 03/P-26)

Description and Function	The storage tank holds blended and filtered feed supplement 7a media at 4°C until further use.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Wet Media	650	0.00
Characteristics	Volume:	850 L	
	Working Capacity:	80%	
	Material:	Stainless Steel 316	
	Height/Diameter Ratio:	2/1	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	4°C	
	Pressure:	2 bar	
Purchase Cost	Storage Tank:	$25,600	

Storage Tank (PFD 03/P-29)

Description and Function	The storage tank holds blended and filtered feed supplement 7b media at 4°C until further use.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Wet Media	65.0	0.00
Characteristics	Volume:	90 L	
	Working Capacity:	80%	
	Material:	Stainless Steel 316	
	Height/Diameter Ratio:	2/1	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	4°C	
	Pressure:	2 bar	
Purchase Cost	Storage Tank:	$12,700	

2,000 L Single-Use Seed Bioreactor (PFD 03/P-37)

Description and Function

The 2000L Xcellerex XDR Bioreactor is used for cell growth to peak density followed by maximum product formation The single-use system is equipped with a jacketed bioreactor vessel, gas mixing cabinet, control console, and cell bags. The bags are disposable and pre-sterilized. The system also offers high level sensors and automated control for temperature, liquid transfer, dissolved oxygen, and pH. Four of these bioreactors operate in parallel.

Vendor

GE Healthcare and Life Sciences

Operation

Batch

Materials Handled

	Input (kg/batch)	**Output (kg/batch)**
Cells	0.00162	7.35
Wet Media	250	1560
Product	0.00	40.1

Characteristics

Model:	Xcellerex XDR-2000 system
Height/Diameter Ratio:	1.5/1
Impeller Type, Angle:	4 blades, 40° pitch
Impeller/Bag Diameter Ratio:	0.34
Bag Size:	2000 L
Sterilization:	Plastic, Disposable

Operation Conditions

Temperature:	36.5°C
Pressure:	2 bar
pH:	7.1
dO_2:	40%
Agitation:	110 rpm
Duration:	19 days

Purchase Cost

Bioreactor with control:	$250,000
Disposable Cellbag:	$2,500

Peristaltic Pumps (PFD 03/P-2,4,6,8,10,12,14,16,18,20,22,24,28,30,32,34,36,38)

Description and Function	The pumps are used to transfer media and cells for upstream bioreaction steps. The pumps are sterile and designed for shear-sensitive biopharmaceutical applications.	
Vendor	Watson-Marlow	
Operation	Batch	
Characteristics	Model:	825 series
	Pumphead Material:	Aluminum alloy
	Support and Frame Material:	Stainless steel 304
	Maximum Flow Rate:	33 L/min
	Maximum Pressure:	3.5 bar
	Sterilization:	CIP, SIP
Operation Conditions	Pressure:	3 bar
	Flow Rate:	Variable (0.1-33 L/min)
Purchase Cost	Pump:	$3,000

Centrifuge (PFD 04/P-39)

Description and Function: This centrifuge will separate the cells from the cell culture liquid that has the solubilized monoclonal antibody product.

Vendor: GEA

Operation: Continuous

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	75.4	0
Media	0	0
Water	1560	1560
Product	10.0	9.62

Characteristics

Model:	CSC 20
Centrifuge Type:	Disc Stack Centrifuge
Material:	Stainless Steel 316
Capacity Range:	500-1000 L/h
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Throughput:	780 L/h

Purchase Cost

Centrifuge:	$1,200,000

Storage Tank 6 (PFD 04/P-41)

Description and Function	This storage tank will collect the liquid product from the centrifuge.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Cells	0	0
	Media	0	0
	Water	1560	1560
	Product	9.62	9.62
Characteristics	Material:	Stainless Steel 316 L	
	Volume:	2,000L	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	25°C	
	Pressure:	1 bar	
Purchase Cost	Tank:	$35,857	

Depth Microfiltration Unit (PFD 04/P-43)

Description and Function: The depth filter is used to remove larger particles not removed from centrifugation. It has two distinct layers with different pore sizes (0.1-1μm) to avoid plugging and increase filter capacity.

Vendor: Millipore Sigma

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Water	1560	1560
Product	9.62	9.34

Characteristics

Model:	Millistak Pod Filter
Filter:	X0HC
Protein Throughput:	21 L/min/m^2
Max. Differential Pressure:	2.1 bar
Max. Operating Pressure:	3.5 bar
Filter effective area:	1.1 m^2
Unit Sterilization:	SIP
Filter Sterilization:	Disposable

Operation Conditions

Temperature:	25°C
Operating Pressure:	1 bar

Purchase Cost

Filter Housing:	$29,200
Filter:	$750 each

Storage Tank 7 (PFD 04/P-45)

Description and Function	This storage tank will collect the filtrate liquid from the depth filtration unit.		
Operation	Batch		
Materials Handled		Input (kg/batch)	Output (kg/batch)
	Cells	0	0
	Media	0	0
	Water	1560	1560
	Product	9.34	9.34
Characteristics	Material:	Stainless Steel 316	
	Volume:	2,000L	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	25°C	
	Pressure:	1 bar	
Purchase Cost	Tank:	$35,900	

Protein A Chromatography Column (PFD 04/P-47)

Description and Function: The Protein A Chromatography column uses a resin that selectively binds the monoclonal antibody product. This step is the first isolation step in the purification process and is useful in eliminating host cell proteins, DNA, cell culture media components.

Vendor: GE Healthcare Life Sciences

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Centrifuge effluent	1560	0
Equilibration buffer	1700	0
Wash buffer	200	0
Elution buffer	750	750
Regeneration buffer	600	0
CIP buffer	800	0
Protein A waste	0	4860
Product	9.34	8.59

Characteristics

Model:	Chromaflow 1000/100-300
Column Diameter:	1.0 m
Bed Height:	0.25 m
Material of Construction:	Stainless Steel 316 L
Bed Volume:	200 L
Resin:	MabSelect Sure LX
Binding Capacity:	50 g mAB/L resin
Working Linear Velocity:	250-400 cm/hr
pH Stability:	3-12
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Column:	$250,000
Resin:	$8,000/liter

Storage Tank 8 (PFD 04/P-49)

Description and Function	This storage tank will collect the eluent from the Protein A Chromatography column.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Cells	0	0
	Media	0	0
	Water	750	750
	Product	8.59	8.59
Characteristics	Material:	Stainless Steel 316	
	Volume:	1,000L	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	25°C	
	Pressure:	1 bar	
Purchase Cost	Tank:	$26,600	

Ultrafiltration/Diafiltration Unit (PFD 04/P-51)

Description and Function: This unit is used for buffer exchange to raise the pH of the solution and concentrate it by 5 times. It is done using tangential flow filtration.

Vendor: Millipore Sigma

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Water	750	150
Product	8.59	8.33

Characteristics

Model:	Cogent® TFF System
Protein Throughput:	21 L/min/m^2
Max. Operating Pressure:	6.8 bar
Filter effective area:	1.1 m^2
Unit Sterilization:	SIP
Filter Sterilization:	Disposable

Operation Conditions: Temperature: 25°C

Purchase Cost

Filter Housing:	$500,000
Filter:	$3600/filter

Storage Tank 9 (PFD 04/P-53)

Description and Function: This storage tank will collect the retentate from the diafiltration operation.

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Water	150	150
Product	8.33	8.33

Characteristics

Material:	Stainless Steel 316
Volume:	500L
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost: Tank: $22,600

Cation Exchange Chromatography Column (PFD 04/P-55)

Description and Function: The cation exchange chromatography column binds positively charged proteins and is used eliminate DNA, some host cell proteins, and leached Protein A.

Vendor: GE Healthcare Life Sciences

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Diafiltration effluent	150	0
Equilibration buffer	800	0
Wash buffer	800	0
Elution buffer	320	320
Regeneration buffer	320	0
CIP buffer	480	0
Cation exchange waste		2550
Product	8.33	7.66

Characteristics

Model:	Chromaflow 1000/100-300
Column Diameter:	1.0 m
Bed Height:	0.2 m
Material of Construction:	Stainless Steel 316 L
Bed Volume:	160 L
Resin:	Capto S
Binding Capacity:	60 g mAB/L resin
Working Linear Velocity:	200-600 cm/hr
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Column:	$250,000
Resin:	$1,500/1L

Storage Tank 10 (PFD 04/P-57)

Description and Function	This storage tank will collect the eluent from the Cation Exchange Chromatography.		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Cells	0	0
	Media	0	0
	Water	320	320
	Product	7.66	7.66
Characteristics	Material:	Stainless Steel 316	
	Volume:	500L	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	25°C	
	Pressure:	1 bar	
Purchase Cost	Tank:	$22,600	

Virus Filtration Unit (PFD 04/P-59)

Description and Function	The virus filtration unit is used to remove viruses using size based membrane separation.		
Vendor	Sartorius		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Cells	0	0
	Media	0	0
	Water	320	320
	Product	7.66	7.28
Characteristics	Model:	Virosart® CPV	
	Filter effective area:	1.8 m^2	
	Sterilization:	SIP	
	Membrane:	Disposable	
Operation Conditions	Temperature:	25°C	
Purchase Cost	Filter:	$10,000/filter	

Hydrophobic Interaction Chromatography Column (PFD 04/P-61)

Description and Function: The hydrophobic interaction chromatography column is run in flow through mode and removes product and process-related impurities, such as aggregates.

Vendor: Column: GE Healthcare and Life Sciences
Resin: Thermo Fisher Scientific

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Filtrate	320	320
Equilibration buffer	1000	0
Wash buffer	1780	1780
Elution buffer	1000	0
Regeneration buffer	600	0
CIP buffer	1000	0
Cation exchange waste	0	3600
Product	7.28	6.70

Characteristics

Model:	Chromaflow 1000/100-300
Column Diameter:	1.0 m
Bed Height:	0.3 m
Material of Construction:	Stainless Steel 316 L
Bed Volume:	200 L
Resin:	POROS Benzyl Ultra
Working Linear Velocity:	200-500 cm/hr
Sterilization:	CIP/SIP

Operation Conditions

Temperature:	25°C
Pressure:	1 bar

Purchase Cost

Column:	$250,000
Resin:	$3,800/10 L

Storage Tank 11 (PFD 04/P-63)

Description and Function	This storage tank will collect the product stream from the hydrophobic interaction chromatography.		
Operation	Batch		
Materials Handled		Input (kg/batch)	Output (kg/batch)
	Cells	0	0
	Media	0	0
	Water	2100	2100
	Product	6.70	6.70
Characteristics	Material:	Stainless Steel 316	
	Volume:	2,500L	
	Sterilization:	CIP/SIP	
Operation Conditions	Temperature:	25°C	
	Pressure:	1 bar	
Purchase Cost	Tank:	$35,900	

Ultrafiltration/Diafiltration Unit (PFD 04/P-65)

Description and Function	The diafiltration unit is used for buffer exchange for the final solution that the product will be stored in PBS. The ultrafiltration is used to concentrate the solution by 5 times.		
Vendor	Millipore Sigma		
Operation	Batch		
Materials Handled		**Input (kg/batch)**	**Output (kg/batch)**
	Cells	0	0
	Media	0	0
	Water	2100	420
	Product	6.70	6.50
Characteristics	Model:	Cogent® TFF System	
	Protein Throughput:	21 L/min/m^2	
	Filter effective area:	1.1 m^2	
	Sterilization:	SIP	
	Membrane:	Disposable	
Operation Conditions	Temperature:	25°C	
Purchase Cost	Unit:	$500,000	
	Filter:	$3600/filter	

Sterile Filtration Unit (PFD 04/P-67)

Description and Function: The sterile filters are 0.2 μm filters that are used as the final purification step. It is used to create a sterile product before it is frozen and then sent to formulation.

Vendor: Sarotorius

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Water	420	420
Product	6.50	6.30

Characteristics

Model:	Sartopore 2 0.2μm
Membrane Filter Material:	Polyethersulfone (PES)
Max. Differential Pressure:	5 bar at 20°C
Filtration Area:	1.8 m^2
Unit Sterilization:	SIP
Filter Sterilization:	Disposable

Operation Conditions

Temperature:	25°C
Operating Pressure:	1 bar

Purchase Cost

Filter:	$650/filter

Final Storage (PFD 04/P-69)

Description and Function: The purified product will be stored in 10L containers and stored at -80°C.

Vendor: Thermo Fisher Scientific

Operation: Batch

Materials Handled

	Input (kg/batch)	Output (kg/batch)
Cells	0	0
Media	0	0
Water	420	420
Product	6.30	6.30

Characteristics

Volume:	10 L
Material:	Polycarbonate
Sterilization:	Disposable

Operation Conditions

Temperature:	25°C
Operating Pressure:	1 bar

Purchase Cost

Filter:	$100/container

Pumps (PFD 04/P-40, P-42, P-44, P-46, P-48, P-50, P-52, P-54, P-56, P-58, P-60, P-62, P-64, P-66)

Description and Function	The pumps are used to transfer liquid. These are high-flow hygienic pumps that are designed for low-shear sanitary pumping. They are ideal for viscous or shear sensitive products.	
Vendor	Watson-Marlow	
Operation	Batch	
Characteristics	Model:	840 Peristaltic Pump
	Pumphead Material:	Aluminum Alloy
	Flow Rate:	65-8140 L/hr
	Max Pressure:	3.5 bar
	Sterilization:	CIP/SIP
Operation Conditions	Temperature:	25°C
	Power:	0.55-3 kW
Purchase Cost	Pump:	$3000

17. Equipment Cost Summary

17.1 Large Production Bioreactor Design Equipment

Inoculum Preparation				
PFD 01	**Type**	**Specification**	**Vendor**	**Purchase Cost**
P-8	Pump	825 series	Watson- Marlow	$3,000
P-9	WAVE Bioreactor	25 L	GE Healthcare Life Sciences	$1,000
P-10	Pump	825 series	Watson- Marlow	$3,000
P-1	Blending Tank	75 L		$12,500
P-2	Pump	825 series	Watson- Marlow	$3,000
P-4	Pump	825 series	Watson- Marlow	$3,000
P-5	Storage Tank	75 L		$12,500
P-6	Pump	825 series	Watson-Marlow	$3,000

Seed Bioreactions				
PFD 01	**Type**	**Specification**	**Vendor**	**Purchase Cost**
P-29	WAVE Bioreactor	100 L	GE Healthcare Life Sciences	$90,000
P-30, 31	Pump	150S	QuattroFlow	$3,000
P-32, 33	WAVE Bioreactor	500 L	GE Healthcare Life Sciences	$300,000
P-34, 35	Pump	825 series	Watson- Marlow	$3,000
P-36, 37	XDR-2000	2000 L	GE Healthcare Life Sciences	$500,000
P-38, 39	Pump	825 series	Watson- Marlow	$3,000
P-39	Pump	825 series	Watson- Marlow	$3,000
P-11	Blending Tank	4000 L		$51,000
P-12	Pump	825 series	Watson- Marlow	$3,000
P-14	Pump	825 series	Watson- Marlow	$3,000
P-15	Storage Tank	4000 L		$51,000
P-16	Pump	1200S 5˚	QuattroFlow	$4,000
P-17	Blending Tank	7000 L		$63,200
P-18	Pump	825 series	Watson- Marlow	$3,000
P-20	Pump	825 series	Watson- Marlow	$3,000
P-21	Storage Tank	250 L		$18,000
P-22	Pump	1200S 5˚	QuattroFlow	$4,000
P-23	Blending Tank	700 L		$24,300
P-24	Pump	825 series	Watson- Marlow	$3,000
P-26	Pump	825 series	Watson- Marlow	$3,000
P-27	Storage Tank	25 L		$9,200
P-28	Pump	150S	QuattroFlow	$3,000

Production Bioreactions				
PFD 01	**Type**	**Specification**	**Vendor**	**Purchase Cost**
P-52	Stainless Steel Bioreactor	20,000 L	GEA	$1,500,000
P-40	Pump	825 series	Watson- Marlow	$3,000
P-41	Storage Tank	7500 L		$69,400
P-42	Pump	825 series	Watson- Marlow	$3,000
P-43	Pump	825 series	Watson- Marlow	$3,000
P-44	Storage Tank	750 L		$25,500
P-45	Pump	825 series	Watson- Marlow	$3,000
P-46	Blending Tank	6000 L		$59,400
P-47	Pump	825 series	Watson- Marlow	$3,000
P-49	Pump	825 series	Watson- Marlow	$3,000
P-50	Storage Tank	6000 L		$59,400
P-51	Pump	825 series	Watson- Marlow	$3,000

Primary Recovery				
PFD 02	**Type**	**Specification**	**Vendor**	**Purchase Cost**
P-54	Centrifuge	3000 – 6000 L/hr	GEA	$1,500,000
P-55	Pump	840 series	Watson- Marlow	$3,000
P-56	Storage Tank 6	20,000 L		$104,700
P-57	Pump	840 series	Watson- Marlow	$3,000
P-58	Depth Filtration Unit	21 L/min/m^2	Millipore Sigma	$67,300
P-59	Pump	840 series	Watson- Marlow	$3,000
P-60	Storage Tank 7	20,000 L		$104,700
P-61	Pump	840 series	Watson- Marlow	$3,000

Initial Purification				
PFD 02	**Type**	**Specification**	**Vendor**	**Purchase Cost**
P-62	Protein A Column	1.0 m	GE Healthcare Life Sciences	$250,000
P-63	Pump	840 series	Watson- Marlow	$3,000
P-64	Storage Tank 8	5,000 L		$55,100
P-65	Pump	840 series	Watson- Marlow	$3,000
P-66	Diafiltration Unit	750 L/hr	Millipore Sigma	$500,000
P-67	Pump	840 series	Watson- Marlow	$3,000
P-68	Storage Tank 9	2,000 L		$35,900
P-69	Pump	840 series	Watson- Marlow	$3,000
P-70	Cation Exchange Column	1.0 m	GE Healthcare Life Sciences	$250,000
P-71	Pump	840 series	Watson-Marlow	$3,000
P-72	Storage Tank 10	2,000 L		$36,000

Polishing Steps				
PFD 02	**Type**	**Specification**	**Vendor**	**Purchase Cost**
P-73	Pump	840 series	Watson- Marlow	
P-75	Pump	840 series	Watson- Marlow	$2,950
P-76	HIC Column	1.0 m	GE Healthcare Life Sciences	$250,000
P-77	Pump	840 series	Watson- Marlow	
P-78	Storage Tank 11	5,000L		$55,140
P-79	Pump	840 series	Watson- Marlow	$2,950
P-80	Diafiltration	750 L/hr	Millipore Sigma	$500,000
P-81	Pump	840 series	Watson- Marlow	$2,950

Large Production Bioreactor Scheme: Additional Units				
Type	**Specification**	**Units**	**Vendor**	**Purchase Cost**
Orbital Shaker	60 rpm	1	Corning	$900
CO_2 Incubator	5.0% CO_2	1	Thermo Scientific	$7,900
Cryogenic Storage Vessel	Locator 8 90 L liquid N_2	1	Thermolyne	$2,700
CBCU Gas mixer	--	5	GE Healthcare Life Sciences	$5,000
Pump Tubing	MasterFlex	1000	Cole-Parmer	$48,900,000
Product Refrigeration	-80˚C, 33.5 ft^3 900 L capacity	4	Thermo Scientific	$60,300
Biowaste tank	100 L	1		$13,500
Neutralization tank	20,000 L	4		$400,000
Sterile Air Compressor	620 L/min 120 L capacity	10	Greeloy Medical	$7,000
CIP Skids	Up to 3m processes	3	Sani-matic	$300,000
Buffer Transfer Container	5,000 L	10		$359,000

17.2 Small Production Bioreactor Design Equipment

Inoculum Preparation				
PFD 03	**Type**	**Specification**	**Vendor**	**Purchase Cost**
P-8	Pump	825 series	Watson- Marlow	$3,000
P-9	WAVE Bioreactor	25 L	GE Healthcare Life Sciences	$1,000
P-10	Pump	825 series	Watson- Marlow	$3,000
P-1	Blending Tank	300 L		$18,100
P-2	Pump	825 series	Watson- Marlow	$3,000
P-4	Pump	825 series	Watson- Marlow	$3,000
P-5	Storage Tank	300 L		$36,200
P-6	Pump	825 series	Watson-Marlow	$3,000

Seed Bioreactions				
PFD 03	**Type**	**Specification**	**Vendor**	**Purchase Cost**
P-23	WAVE Bioreactor	500 L	GE Healthcare Life Sciences	$150,000
P-24	Pump	825 series	Watson- Marlow	$3,000
P-11	Blending Tank	900 L		$26,000
P-12	Pump	825 series	Watson- Marlow	$3,000
P-14	Pump	825 series	Watson- Marlow	$3,000
P-15	Storage Tank	50 L		$10,700
P-16	Pump		Watson- Marlow	$3,000
P-17	Blending Tank	90 L		$12,700
P-18	Pump	825 series	Watson- Marlow	$3,000
P-20	Pump	825 series	Watson- Marlow	$3,000
P-21	Storage Tank	25 L		$9,100
P-22	Pump		Watson- Marlow	$3,000

Production Bioreactions				
PFD 03	**Type**	**Specification**	**Vendor**	**Purchase Cost**
P-37	XDR-2000	2000 L	GE Healthcare Life Sciences	$250,000
P-31	Blending Tank	1100 L		$28,200
P-32	Pump	825 series	Watson- Marlow	$3,000
P-34	Pump	825 series	Watson- Marlow	$3,000
P-35	Storage Tank	1100 L		$28,200
P-36	Pump	825 series	Watson- Marlow	$3,000
P-25	Pump	825 series	Watson- Marlow	$3,000
P-26	Storage Tank	850 L		$51,200
P-27	Pump	825 series	Watson- Marlow	$3,000
P-28	Pump	825 series	Watson- Marlow	$3,000
P-29	Storage Tank	90 L		$25,400
P-30	Pump	825 series	Watson- Marlow	$3,000

Primary Recovery				
PFD 04	**Type**	**Specification**	**Vendor**	**Purchase Cost**
P-39	Centrifuge	500 – 1000 L/hr	GEA	$1,200,000
P-40	Pump	840 series	Watson- Marlow	$2,950
P-41	Storage Tank 6	2,000 L		$35,857
P-42	Pump	840 series	Watson- Marlow	$2,950
P-43	Depth Filtration Unit	21 L/min/m^2	Millipore Sigma	$29,160
P-44	Pump	840 series	Watson- Marlow	$2,950
P-45	Storage Tank 7	2,000 L		$35,857
P-46	Pump	840 series	Watson- Marlow	$2,950

Initial Purification				
PFD 04	**Type**	**Specification**	**Vendor**	**Purchase Cost**
P-47	Protein A Column	1.0 m	GE Healthcare Life Sciences	$250,000
P-48	Pump	840 series	Watson- Marlow	$2,950
P-49	Storage Tank 8	1,000 L		$26,567
P-50	Pump	840 series	Watson- Marlow	$2,950
P-51	Diafiltration Unit	750 L/hr	Millipore Sigma	$500,000
P-52	Pump	840 series	Watson- Marlow	$2,950
P-53	Storage Tank 9	500L		$22,550
P-54	Pump	840 series	Watson- Marlow	$2,950
P-55	Cation Exchange Column	1.0 m	GE Healthcare Life Sciences	$250,000
P-56	Pump	840 series	Watson-Marlow	$2,950
P-57	Storage Tank 10	2,000 L		$35,857

Polishing Steps				
PFD 04	**Type**	**Specification**	**Vendor**	**Purchase Cost ($/batch)**
P-58	Pump	840 series	Watson- Marlow	
P-60	Pump	840 series	Watson- Marlow	$2,950
P-61	HIC Column	1.0 m	GE Healthcare Life Sciences	$250,000
P-62	Pump	840 series	Watson- Marlow	
P-63	Storage Tank 11	2,500 L		$38,704
P-64	Pump	840 series	Watson- Marlow	$2,950
P-65	Diafiltration	750 L/hr	Millipore Sigma	$500,000
P-66	Pump	840 series	Watson- Marlow	$2,950

Small Production Bioreactor Scheme: Additional Units				
Type	**Specification**	**Units**	**Vendor**	**Purchase Cost**
Orbital Shaker	60 rpm	1	Corning	$900
CO_2 Incubator	5.0% CO_2	1	Thermo Scientific	$7,900
Cryogenic Storage Vessel	Locator 8 90 L liquid N_2	1	Thermolyne	$2,700
CBCU Gas mixer	--	5	GE Healthcare Life Sciences	$5,000
Pump Tubing	MasterFlex	1000	Cole-Parmer	$48,900,000
Product Refrigeration	-80˚C, 33.5 ft^3 900 L capacity	3	Thermo Scientific	$45,200
Biowaste tank	50 L	1		$10,700
Neutralization tank	20,000 L	2		$200,000
Sterile Air Compressor	620 L/min 120 L capacity	6	Greeloy Medical	$4,200
CIP Skids	Up to 3m processes	3	Sani-matic	$300,000
Buffer Transfer Container	1,000 L	10		$265,000

Additional Equipment Included in Annual Expenses for Both Designs		
Type	**Units**	**Vendor**
Water-glycol heater	1	Chromalox
Water heater	2	PVI Industries, LLC
Cooling water unit	2	Cole-Parmer
Biosafety Cabinet	2	Thermo Scientific
WFI Still	1	
Clean Steam Generator	1	Spirax Sarco
Filter Integrity Test	1	Millipore
Water Treatment Package	1	MECO
Biowaste Inactivation System	1	
Waste Neutralization System	1	
Quality Control Lab	1	

18. Scheduling

Scheduling and process duration is important to consider for both the design and operation of biopharmaceutical plants. Both the Large and Small Production Bioreactor Schemes require 24-hour operation and supervision.

Tables 18.1 and 18.2 illustrate the Gantt chart and schedules for the Large Production Bioreactor Scheme and Small Production Bioreactor Scheme, respectively. For the Large Production Bioreactor Scheme, the batch time is 45 days and 14 hours with the start of each batch occuring every 21 days and 13 hours. Since this scheme produces 25.2 kg per batch, four batches will be required to reach the production goal of 100 kg of mAb per year. Therefore, the total time required to reach the production goal is 111 days and 4 hours, or approximately 4 months. For the Small Production Bioreactor Scheme, the batch time is 30 days and 8 hours with the start of each batch occuring every 9 days and 4 hours. Both the batch and cycle time are shorter for than for the Large Production Bioreactor Scheme, however this smaller scheme is designed to produce only 6.3 kg per batch. This requires a total of sixteen batches to reach the annual production goal. The total time to complete sixteen batches is 178 days and 13 hours, or approximately 6 months.

The major headings of the combined upstream and downstream processes are labeled on the left as: Inoculum Preparation, Seeding, Production, Primary Recovery, Purification, and Polishing. These headings correspond to the titles in the block flow diagrams in Figures 10.1 and 10.2 in Section 10. Scheduled units are labeled in accordance with the corresponding labels on the computer-drawn flowsheets in Figures 12.1 through 12.6 and with descriptive labels for simplicity. Each color indicates a new batch.

Although the Small Production Bioreactor Design takes longer, the smaller production volume actually results in higher product quality and lower batch risk, as discussed in Section 2.2. The smaller design also provides more scalability with the capability to produce quantities between 6.30 and 201 kg annually. Comparatively, the larger design produces quantities between 25.2 kg and 302 kg annually. Given the projected sales forecast of OCREVUS, both schemes can match the maximum required annual mAb production for the duration of the patent. Likewise, in an off-patent scenario, it is unlikely that annual production will exceed that of the on-patent market, since competitors reduce the market available for sales. A specific, detailed economic analysis of the advantages and disadvantages of each scheme will be discussed in Section 21.

Table 18.1 Gantt chart for the Large Production Bioreactor Process (PFD 01 and PFD 02).

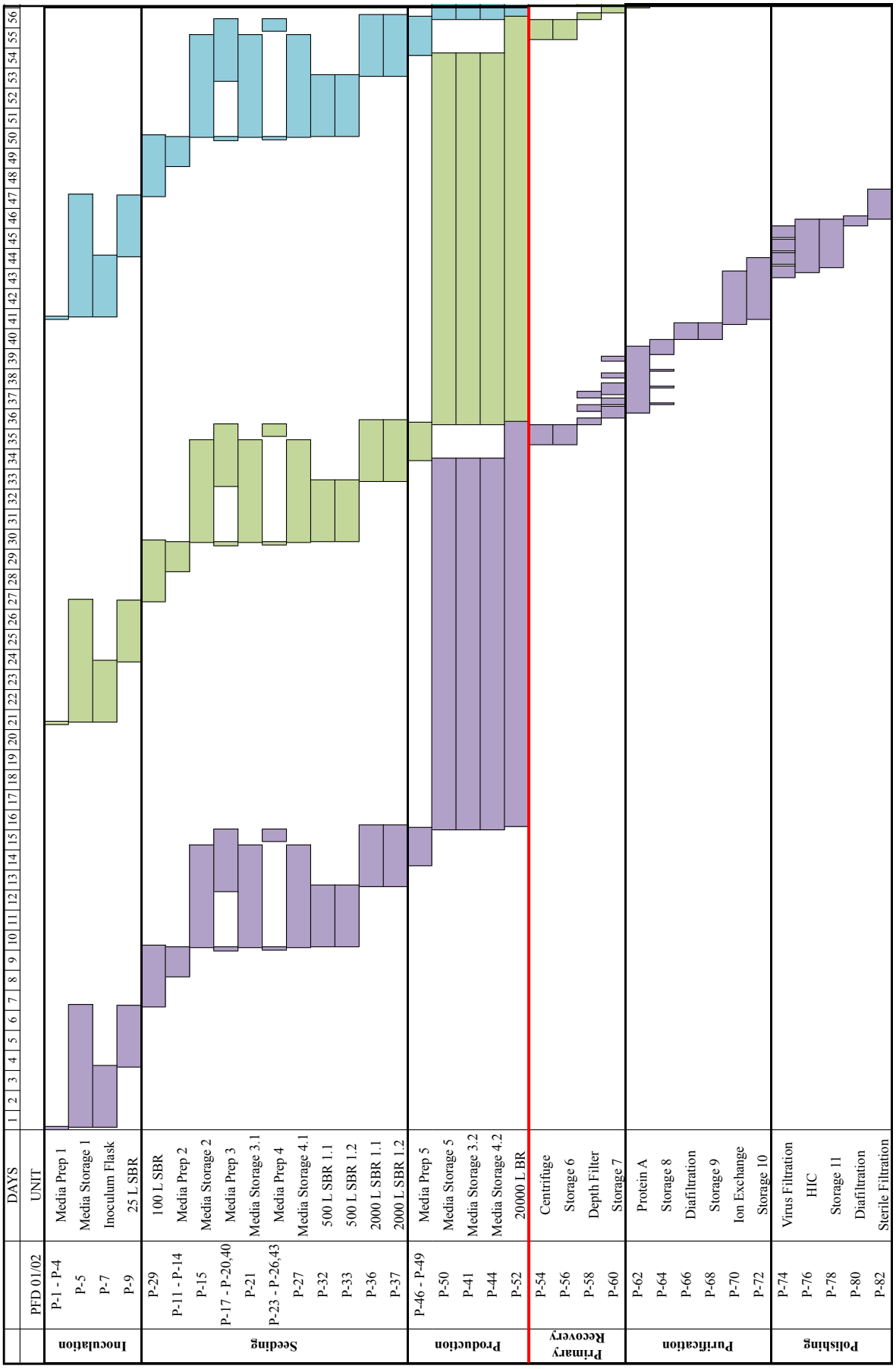
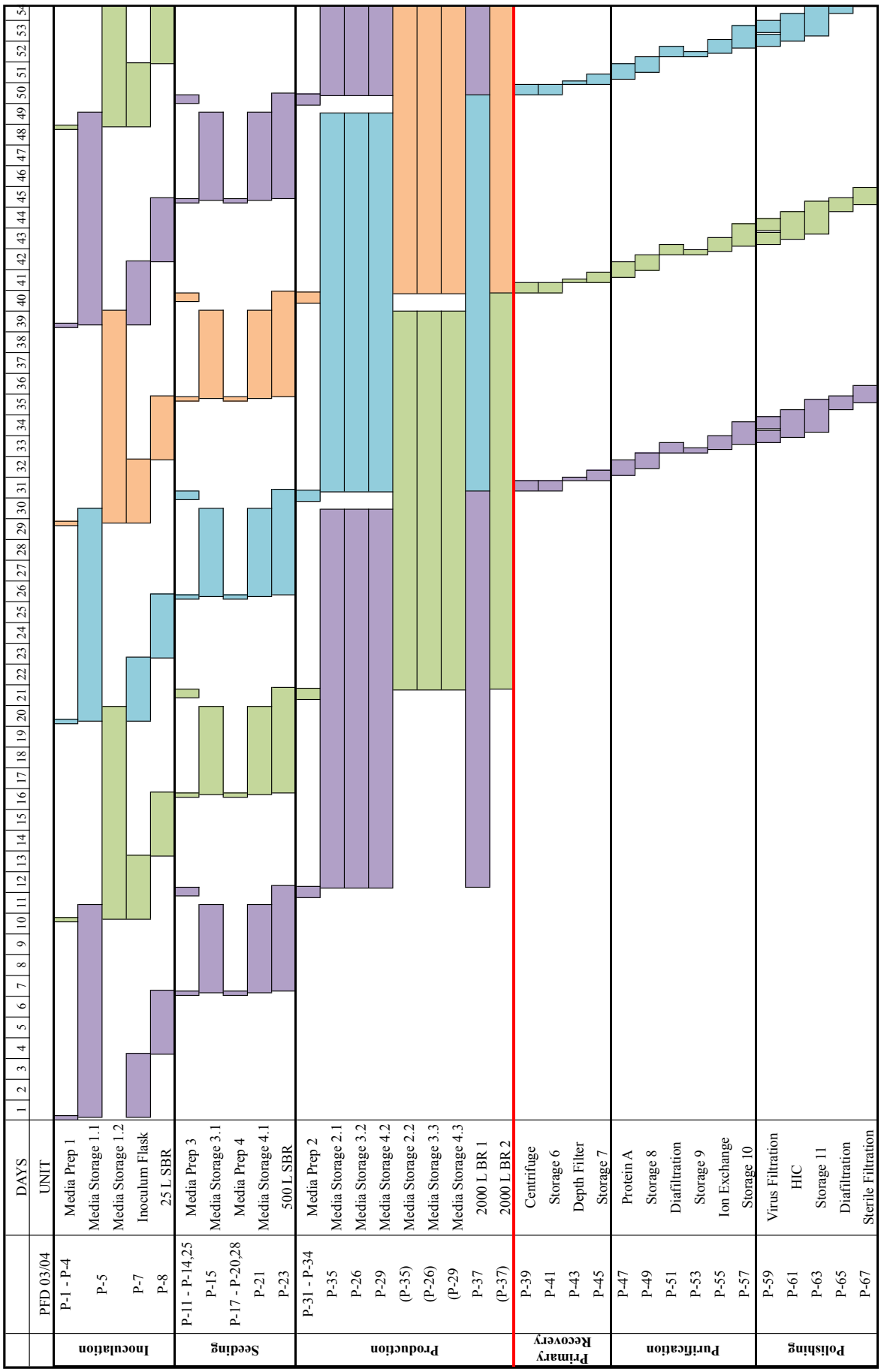


Table 18.2 Gantt chart for the Small Production Bioreactor Process (PFD 03 and PFD 04).



19. Fixed-Capital Investment Summary

Assuming that this plant is part of a pre-existing plant, only 4-6 months out of the year will be dedicated to Ocrevus production. During this time, production will take place 24 hours per day, 7 days per week in four shifts. Eight operators will be working in any given shift and will be paid $42 per hour. Technical assistance will be provided by engineers and control laboratory staff. These labor costs amount to about $1.3 million (MM) per large batch. Other fixed costs include Maintenance and Overhead items which can be modeled as a fraction of wages and depreciable capital. These costs total to about $3.1 MM per large bioreactor batch of 25 kg mAb and $1.8 MM per small bioreactor batch of 6.3 kg mAb.

The total investment required prior to the start of production is about $33.6 MM for the large bioreactor scheme and $19.4 MM for the small bioreactor scheme. This includes the total bare module costs of all equipment units, site preparations and service facilities, as well as any contingencies and start-up costs. The bare module factor accounts for the costs of installation materials and labor, freight and insurances, as well as construction overhead. While the factor for a typical chemical engineering plant is around 3.21, a slightly lower factor will be used for this process because most of the equipment is highly specialized for biopharmaceutical applications and is easy to install. An average bare module factor of 2.8 will be used for all equipment cost estimations. In the on-patent analysis, all R&D activities and clinical trial costs will also be included in the annual fixed costs.

A summary of the investment is provided in Appendix F.1 and fixed costs are provided in Appendix F.2.

20. Operating Cost- Cost of Manufacture

The operating costs include all raw materials, utilities, and general expenses which scale with the plant productivity. These costs will be incurred annually and on an ongoing basis. Table 20.1 shows the required raw materials for each production batch in the Large Production Bioreactor scheme. Table 20.2 shows the same for the Small Production Bioreactor scheme.

Table 20.1 Raw Materials: Large Production Bioreactor Design

Upstream & Downstream Raw Materials: Large Production Bioreactor				
Raw Materials	**Units**	**Specifications**	**Vendor**	**Purchase Cost ($/batch)**
Cryovials	1	1000/pack	Sigma-Aldrich	$400
Cryogenic storage boxes	3	25/pack	Thermo Scientific	$1,700
Liquid Nitrogen	2	55 gallon drum		$60
ActiPro Powder Medium	302	25 L bottle	GE Healthcare Life Sciences	$311,100
CellBoost 7a Powder Medium	580	10 L bottle	GE Healthcare Life Sciences	$1,044,000
CellBoost 7b Powder Medium	58	10 L bottle	GE Healthcare Life Sciences	$194,900
Antifoam	50	2.5 L bottle	GE Healthcare Life Sciences	$8,500
L-glutamine	100	500 mL bottle	Millipore Sigma	$3,000
Sodium Hydroxide Pellets	25	35 kg drum	Millipore Sigma	$640,000
Sodium Bicarbonate	1	45 kg drum	Millipore Sigma	$900
Propylene Glycol	6	55 gal drum	Dow Chemical Company	$4,200
CHO Cell vials	1	1 mL per vial $3x10^5$ cells/mL	Thermo Fisher Scientific	$600
Media Filters	7	Opticap XLT 10 0.57 m^2, 0.2µm	Millipore Sigma	$2,800
Shake Flask	1	50 mL	Corning	$8.00
Shake Flask	1	250 mL 6/pack	Corning	$160.00

Shaker Flask Clamp	1		Eppendorf	$40
Cellbag	1	22 L	GE Healthcare Life Sciences	$500
Cellbag	1	100 L	GE Healthcare Life Sciences	$800
Cellbag	2	500 L	GE Healthcare Life Sciences	$2,000
XDR-200 Probag	2	2000 L	GE Healthcare Life Sciences	$5,000
Air Filters	10	Durapore 0.69m^2, 0.22 µm	GE Healthcare Life Sciences	$4,000
Depth Filters	90	Millistak Pod 1.1 m^2	Millipore Sigma	$67,400
Protein A Resin	200	MabSelect Sure LX 1 L bottle	GE Healthcare Life Sciences	$1,600,000*
Protein A Buffers	--	16400 L	Millipore Sigma	$16,200
Diafiltration Filters	2	Pellicon 2 Cassettes 30 kDa	Millipore Sigma	$7,200
Tromethamine Diafiltration Buffer	1	50 kg	Sigma-Aldrich	$5,700
PBS Diafiltration Buffer	700	1 L bottle	Millipore Sigma	$23,000
Capto S Cation Ex. Resin	16	10 L bottle	GE Healthcare Life Sciences	$240,000*
Cation Ex. Buffers	--	10900 L	Millipore Sigma	$15,200
Virus Filters	4	Virosart CPV	Sartorius	$40,300
HIC Resin	20	Poros Benzyl Ultra 10 L bottle	Thermo Fisher Scientific	$76,000*
HIC Buffers		16610 L	Millipore Sigma	$13,300
Diafiltration Filters	2	Pellicon 2 Cassettes 30 kDa	Millipore Sigma	$7,200
Sterile Filters	70	Sartopore 0.2 µm	Sartorius	$45,500
Biotainers	70	Nalgene 10 L	Thermo Fisher Scientific	$7,100
Bleach	--	56700 L		$153,400
Autoclave bags	160	2.5 L	Thermo Fisher Scientific	$400

Table 20.2 Raw Materials: Small Production Bioreactor Design

Upstream & Downstream Raw Materials: Small Production Bioreactor				
Raw Materials	**Units**	**Specifications**	**Vendor**	**Purchase Cost ($/batch)**
Cryovials	1	1000/pack	Sigma-Aldrich	$400
Cryogenic storage boxes	3	25/pack	Thermo Scientific	$1,700
Liquid Nitrogen	2	55 gallon drum		$60
ActiPro Powder Medium	45	25 L bottle	GE Healthcare Life Sciences	$45,700
CellBoost 7a Powder Medium	70	10 L bottle	GE Healthcare Life Sciences	$125,100
CellBoost 7b Powder Medium	7	10 L bottle	GE Healthcare Life Sciences	$23,500
Antifoam	10	2.5 L bottle	GE Healthcare Life Sciences	$440
L-glutamine	100	500 mL bottle	Millipore Sigma	$3,000
Sodium Hydroxide Pellets	1	35 kg drum	Millipore Sigma	$700
Sodium Bicarbonate	1	45 kg drum	Millipore Sigma	$900
Propylene Glycol	1	55 gal drum	Dow Chemical Company	$800
CHO Cell vials	1	1 mL per vial $3x10^5$ cells/mL	Thermo Fisher Scientific	$600
Media Filters	6	Opticap XLT 10 0.57 m^2, 0.2µm	Millipore Sigma	$2,400
Shake Flask	1	50 mL	Corning	$8.00
Shake Flask	1	250 mL 6/pack	Corning	$160
Shaker Flask Clamp	1		Eppendorf	$40.00
Cellbag	1	22 L	GE Healthcare Life Sciences	$500
Cellbag	1	500 L	GE Healthcare Life Sciences	$1,000
XDR-200 Probag	1	2000 L	GE Healthcare Life Sciences	$2,500
Air Filters	10	Durapore 0.69m^2, 0.22 µm	GE Healthcare Life Sciences	$4,000

Depth Filters	8	Millistak Pod 1.1 m^2	Millipore Sigma	$6,000
Protein A Resin	200	MabSelect Sure LX 1 L bottle	GE Healthcare Life Sciences	$1,600,000*
Protein A Buffers	--	4100 L	Millipore Sigma	$4,000
Diafiltration Filters	1	Pellicon 2 Cassettes 30 kDa	Millipore Sigma	$14,000
Tromethamine Diafiltration Buffer	1	25 kg	Sigma-Aldrich	$800
PBS Diafiltration Buffer	420	1 L	Millipore Sigma	$13,900
Capto S Cation Ex. Resin	16	10 L bottle	GE Healthcare Life Sciences	$240,000*
Cation Ex. Buffers	--	2720 L	Millipore Sigma	$3,800
Virus Filters	1	Virosart CPV	Sartorius	$10,000
HIC Resin	23	Poros Benzyl Ultra 10 L bottle	Thermo Fisher Scientific	$89,000*
HIC Buffers		5380L	Millipore Sigma	$4,300
Diafiltration Filters	1	Pellicon 2 Cassettes 30 kDa	Millipore Sigma	$3,600
Sterile Filters	42	Sartopore 0.2 µm	Sartorius	$27,300
Biotainers	42	Nalgene 10 L	Thermo Fisher Scientific	$4,300
Bleach	--	1400 L		$3,600
Autoclave bags	160	2.5 L	Thermo Fisher Scientific	$200

21. Profitability Analyses- Business Case

In order to validate the feasibility of these proposed process designs, a detailed profitability analysis has been performed. It is assumed that a 15% internal rate of return (IRR) will be desired within five years of the production start date. Production Year (PY) 5 has been selected as the reasonable time point by which a return would be desired, and also provides a uniform frame of reference for comparing all schemes. An effective tax rate of 37% has been used for all analyses. These constraints allow the required selling price of the mAb to be determined, and the superior design scheme to be selected.

The two process designs have been evaluated using two separate frameworks. The first is the "off-patent" analysis, in which only the capital costs and operating costs are considered in the economic evaluation. All R&D expenditures are exempt from the cash flow construction. This represents the expenditures incurred by a company that is trying to manufacture a generic drug from an existing drug whose patent has recently expired.

The second is the "on-patent" analysis, in which the R&D expenditures, extended timeline, and probability of success of the drug has been factored in. In this case, the 15% IRR needs to be achieved before the patent expiration date.

The Sales Forecast (Section 4) constructed from historical market data implies rapid uptake in the first few years, with a slight, small annual growth rate after about six years of production. Translating the sales forecast to the mass of mAb allows the required annual production capacity to be determined. This calculation has been performed using the market selling price of Ocrevus, at $65,000 per 1200 mg annual treatment. The results of this analysis are shown in Table 21.1.

Table 21.1 Annual Production Requirements

YEAR	Forecasted Ocrevus Sales ($MM)	Treatments Administered	mAb Required (kg)
1	1,377	21,180	25
2	3,331	51,250	62
3	5,397	83,030	100
4	6,908	106,280	128
5	7,737	119,030	143
6	8,666	133,320	160
7	8,839	135,980	163
8	9,016	138,700	166
9	9,196	141,480	170
10	9,380	144,310	173

These production requirements determine how capacity is expected to scale up from year to year and has been factored into the operating costs on the cash flow analysis.

The desired internal rate of return (IRR) is 15%, which represents the percentage rate earned on each dollar invested within a given time frame. This can be calculated by calculating the net present value (NPV) of all cash flows using a discount rate equivalent to the IRR. The formula for NPV is,

$$NPV = \sum_{t=1}^{T} \frac{C_t}{(1+r)^t} - C_o$$

where C_t is the cumulative cash flow at year t, C_o is the total initial investment, r is the discount rate, and t is the number of years. The year at which the cumulative NPV is equal to 0, or become positive, is the "breakeven" year, representing to year at which the IRR has been earned.

21.1 Off-Patent Analysis

In the off-patent analysis, it has been assumed that the project timeline starts in 2018. Year 1 is dedicated to plant set-up and capital investment, while the first year of operations and sales is Year 2, or 2019. As explained in the patent analysis (Section 9), the price of a physician-administered drug drops between 38 and 48% following patent expiration.[16] For this reason, a conservative selling price of $35,000, or a reduction of 46% has been used in the off-patent profitability analyses.

21.1.1 Large Production Bioreactor Design

An economic evaluation of the Large Production Bioreactor Design under this framework shows that a 15% IRR on the $33.6 MM initial investment cannot be earned within 5 years. Using the baseline price tag of $35,000 per 1200 mg treatment, the desired 15% IRR can be achieved by 2024, or the sixth year of production. At the end of Production Year 10, the cumulative Net Present Value (NPV) is about $9.1 billion. Though the desired outcome is not achieved, this is still a profitable scenario and can be explored and optimized further to achieve the desired return. A summarized cash flow analysis is shown in Table 21.2. The complete cash flow sheet for this analysis is shown in Appendix F.4.1

Table 21.2 Condensed Cash Flow for Off-Patent Large Production Bioreactor Design

YEAR	Cash Flow ($MM)	Cumulative NPV at 15% IRR ($MM)
2018	-3,093	-3,093
2019	-1,516	-4,411
2020	-890	-5,085
2021	1,532	-4,077
2022	3,171	-2,264
2023	3,775	-387
2024	5,199	1,860
2025	5,734	4,016
2026	5,850	5,929
2027	5,967	7,625
2028	6,087	9,130

21.1.2 Small Production Bioreactor Design

Since the Small Production Bioreactor Design requires a smaller equipment and thus a reduced capital investment, the outcome from this analysis is slightly more profitable. Using the same baseline price of $35,000 per 1200 mg treatment, the desired 15% IRR on the initial investment of $19.7 MM can be attained before the end of 2022, or the 4th year of production, and the cumulative NPV at the end of PY10 is $12.9 B. A summarized cash flow analysis is shown in Table 21.3. The complete cash flow sheet for this analysis is shown in Appendix F.4.2.

Table 21.3 Condensed Cash Flow for Off-Patent Small Bioreactor Design

YEAR	Cash Flow ($MM)	Cumulative NPV at 15% IRR ($MM)
2018	-1,951	-1,951
2019	-393	-2,293
2020	-46	-2,328
2021	2,205	-878
2022	3,791	-1,289
2023	4,280	3,417
2024	5,279	5,700
2025	5,720	7,850
2026	5,775	9,738
2027	5,951	11,429
2028	6,071	12,930

21.1.3 Price Sensitivity Analysis

The profitability findings reported above reflect the projections for a selling price of $35,000 per 1200 mg treatment. This price estimate may need to be adjusted based on market conditions, competitive products, and the company's financial situation. Figure 21.1 shows how the selling price would affect the return on investment at Production Year (PY) 5 for both design schemes. Figure 21.2 shows the year at which the desired 15% IRR will be attained at different prices. These analyses assume that the sales projections remain constant regardless of price.

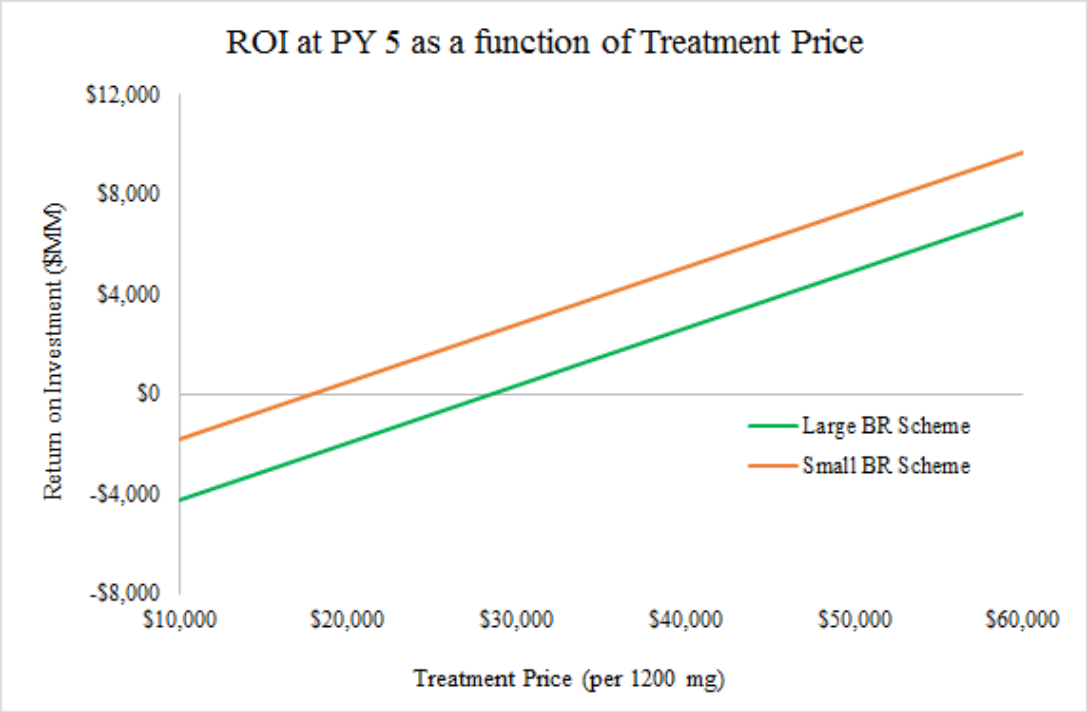


Figure 21.1 Expected Return on Investment at the end of the 5th year of production as a function of treatment price

Figure 21.2 This chart shows the year at which the desired 15% IRR will be achieved as a function of treatment price

21.1.4 Sales Volume Sensitivity Analysis

Another factor that heavily influences the profitability is the sales forecast. The revenues will depend on the number of treatments administered annually, which can only be forecasted from market data. The sales forecast, therefore, is subject to variability and a sensitivity analysis has been conducted to make an educated decision about the price point given the volatility of future market conditions. A range of forecasts has been constructed by multiplying the default annual administered treatments by several factors. Figure 21.3 shows how the sales forecast would affect the return on investment for both design schemes. Figure 21.4 shows how long it will take to achieve a 15% IRR given the range of sales forecasts.

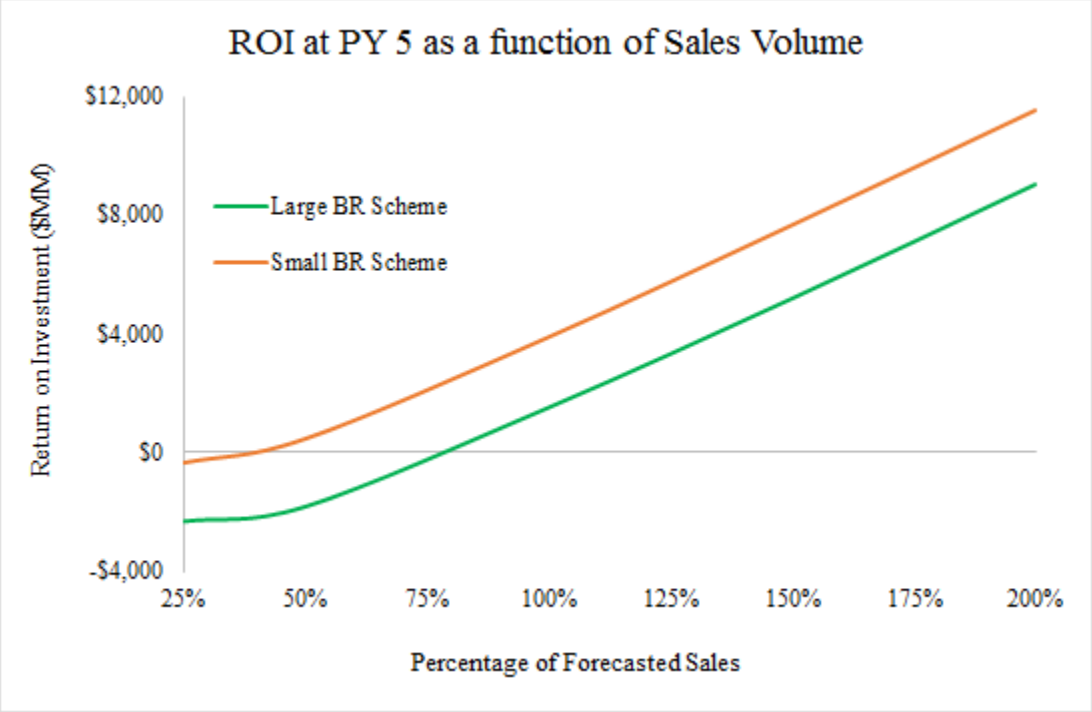


Figure 21.3 This graph shows the expected return on investment at the end of production year 5 as a function of the percentage of forecasted sales truly realized

Figure 21.4 This chart shows the year at which the desired 15% IRR will be attained as a function of the sales forecast factor

21.2 On-Patent Analysis

The on-patent analysis requires evaluating the project over a longer timeline and with several additional cost and logistical considerations. Of all the discovery and development activities undertaken by research institutions and biopharmaceutical companies, very few products are able to ultimately be sold on the market. Many molecules are abandoned early in the development process, while others may fail to pass the final Phase III clinical trials. According to a study conducted by the Tufts Center for the Study of Drug Development, the probability of success for a biopharmaceutical drug is on average 11.83%.[31] Factoring in this low success rate, the effective estimated average pre-tax industry cost for a new prescription drug approval is $2.56 billion, for which the timeline from discovery to market is approximately 128 months. This includes all activities associated with R&D, pilot plant development, and FDA regulated clinical trials. Of the $2.56 billion cost, 30.8% goes towards pre-human expenditures, meaning all activities before the product is tested in human patients. The FDA data for Ocrevus reveals that the clinical trial start date was March 15, 2011 and the final approval date was March 28, 2017. Based on this data, the timeline has been adjusted such that R&D

activities start in 2012, 7 years prior to the production start date. Pre-human expenditures have been spread across the four years from patent filing to the clinical trial start date, while the remaining 69.2% of the cost are incurred during the seven years in clinical trials. The baseline selling price for this framework is $65,000 per annual treatment, which is the Roche list price for the patented drug, Ocrevus.

21.2.1 Large Production Bioreactor Design

In the Large Production Bioreactor Design, the on-patent economic analysis shows that the desired 15% IRR will be achieved by 2023, or Production Year 5. This is earlier than what was found in the off-patent analysis, since the higher investment cost is more than offset by the increased revenues from the higher sales price. By Production Year 10 or 2028, the patent expiration date, the cumulative NPV is $5.3 B. A summarized cash flow analysis is shown in Table 21.4. The complete cash flow sheet for this analysis is shown in Appendix F.4.3.

Table 21.4 Condensed Cash Flow for On-Patent Large Production Bioreactor Design

YEAR	Cash Flow ($MM)	Cumulative NPV at 15% IRR ($MM)
2008	-197	-197
2009	-197	-369
2010	-197	-518
2011	-197	-647
2012	-253	-792
2013	-253	-918
2014	-253	-1,027
2015	-253	-1,122
2016	-253	-1,205
2017	-253	-1,277
2018	-3,093	-2,042
2019	-746	-2,202
2020	-973	-2,020
2021	4,550	-1,280
2022	7,035	-286
2023	8,102	709
2024	10,045	1,783
2025	10,678	2,775
2026	10,892	3,655
2027	11,110	4,436
2028	14,393	5,315

21.2.2 Small Production Bioreactor Design

In the Small Production Bioreactor Design, the on-patent analysis shows a 15% IRR attained by the end of 2022, or Production Year 4. This scheme is slightly more profitable, with an NPV of $6.2 B by 2028. A summarized cash flow analysis is shown in Table 21.5. The complete cash flow sheet for this analysis is shown in Appendix F.4.4.

Table 21.5 Condensed Cash Flow for On-Patent Small Production Bioreactor Design

YEAR	Cash Flow ($MM)	Cumulative NPV at 15% IRR ($MM)
2008	-197	-197
2009	-197	-369
2010	-197	-518
2011	-197	-647
2012	-253	-792
2013	-253	-918
2014	-253	-1,027
2015	-253	-1,122
2016	-253	-1,205
2017	-253	-1,277
2018	-1,951	-1,759
2019	377	-1,678
2020	1,817	-1,338
2021	5,224	-490
2022	7,654	592
2023	8,607	1,650
2024	10,126	2,732
2025	10,663	3,723
2026	10,817	4,597
2027	11,094	5,378
2028	13,249	6,186

21.2.3 Price Sensitivity Analysis

Although the selected sales price is representative of the true market price of Ocrevus, it is possible that the price will need to be adjusted higher or lower depending on the competitive landscape or the company's financial situation. If the 15% IRR needs to be achieved sooner than the current forecast, a higher price tag may be required. Figure 20.5 shows the price sensitivity to the rate of return at PY 4, while Figure 21.6 shows the years required to achieve a 15% IRR at a range of selling points.

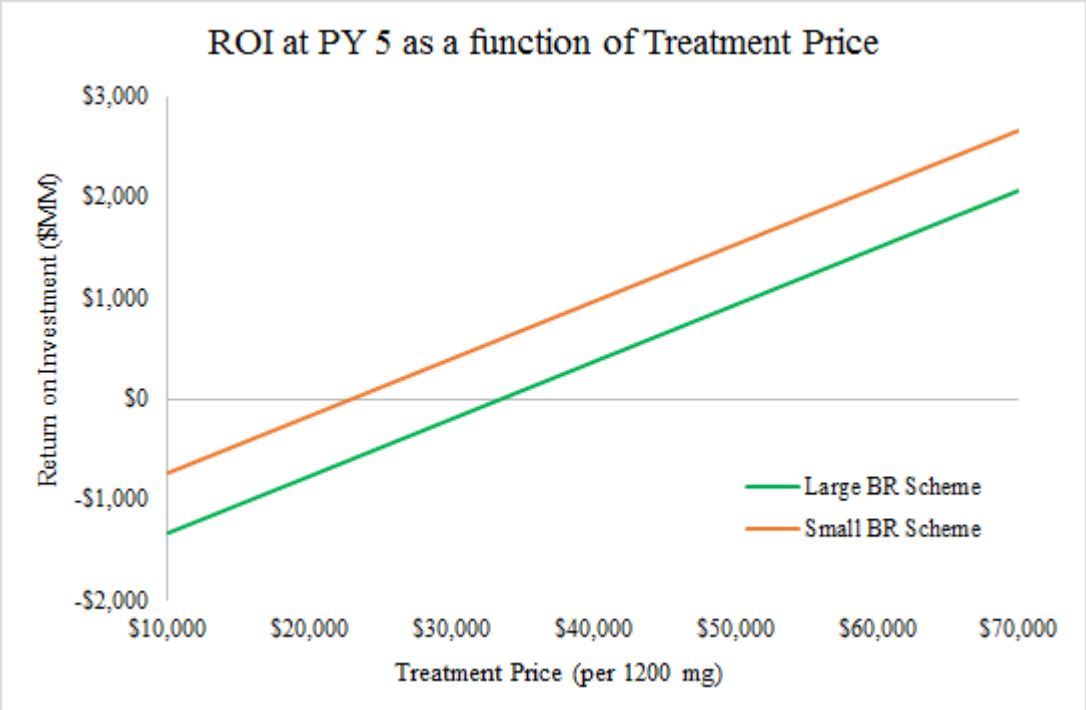


Figure 21.5 Expected Return on Investment at the end of the 5th year of production as a function of treatment price

Figure 21.6 This graph shows the year at which the desired 15% IRR will be achieved as a function of the treatment sales price

21.2.4 Sales Volume Sensitivity Analysis

As was true for the off-patent analysis, the sales forecast is an important factor in the profitability analysis. A range of forecasts has been constructed by assuming the true sales realized are 25%, 50%, 100% 150%, or 200% of the forecasted sales. Figure 21.7 shows how the sales forecast would affect the return on investment for both design schemes. Figure 21.8 shows how long it will take to achieve a 15% IRR given the range of realized sales.

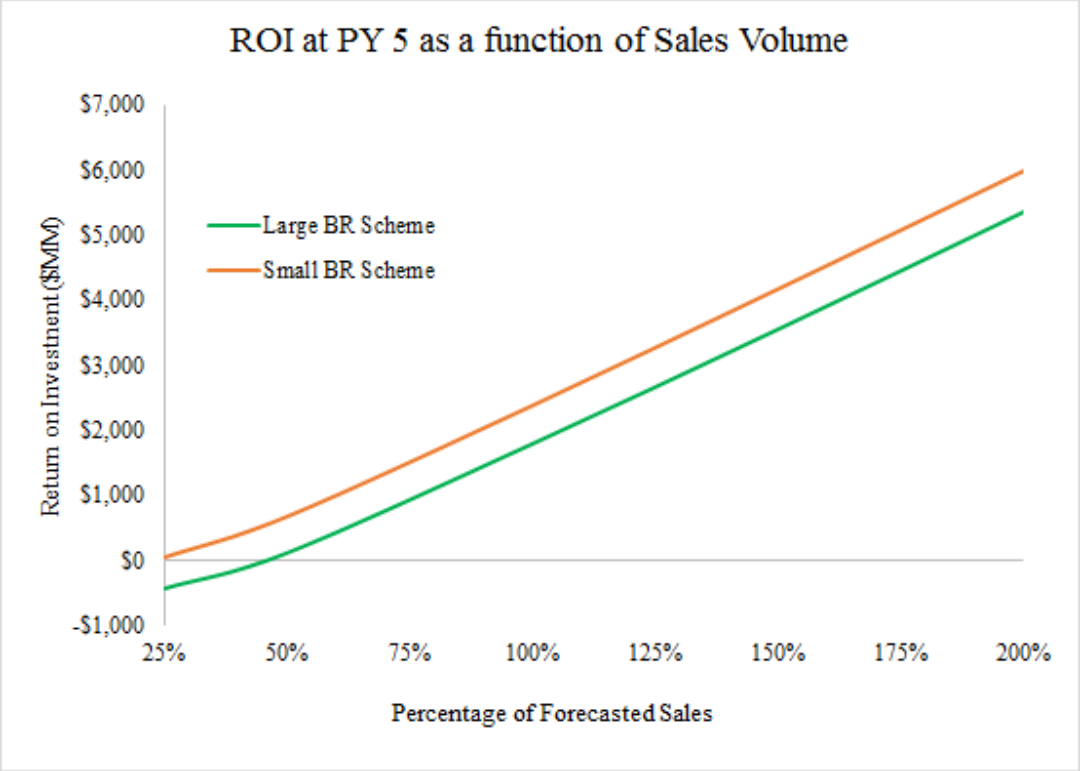


Figure 21.7 This graph shows the expected return on investment at the end of the fifth production year as a function of the percentage of forecasted sales that are actually realized

Figure 21.8 This graph shows the year at which the desired 15% IRR will be attained as a function of the percentage of forecasted sales truly realized

21.3 Summary

From the analyses of the Large and Small Production Bioreactor Designs under both off-patent and off-patent frameworks, it is clear that the Small Production Bioreactor Design is always more profitable. This is attributed to the smaller batch size, which downsizes the required equipment and thus the initial capital investment. Comparing the on-patent and off-patent frameworks, it can be seen that the desired 15% IRR can be earned within a shorter time period in the on-patent analysis, even though there are additional R&D investments required. This can be explained by the selling price of on-patent drugs, which is typically almost double that of the generic, off-patent counterpart.

22. Additional Considerations

22.1 Environmental Impact

The manufacturing process for monoclonal antibodies, or for any biopharmaceutical product, has a sizeable environmental impact in the form of energy and water use and waste disposal. Aqueous wastes such as cell media and purification buffers are the most significant effluents in this process.[32] In order to minimize the associated biohazard, these streams along with the solid cell waste will be inactivated with heat and neutralized through pH adjustment before they can be safely disposed.[33] Further design initiatives could also be taken to explore the possibility of recycling reagents and streams back to the process.

While the power and water consumption for traditional manufacturing processes is quite high, the use of single-use (SU), disposable equipment significantly reduces the carbon footprint of this project. Rigorous comparative analyses indicate that SU bioprocess technologies exhibit lower environmental impact than reusable bioprocessing technologies in all impact categories examined, from terrestrial ecotoxicity to marine eutrophication to ozone depletion. Several life-cycle assessments (LCAs) conducted by ThermoFisher have demonstrated that single-use systems use less water and energy, and have a lower overall environmental impact compared to conventional fixed systems.[34] For a typical commercial mAb production process at 3 x 2,000 L scale, a SU system used 87% less water, 29% less energy, and created 25% less CO_2 emissions than a fixed system. These differences are mainly attributed to the water usage and energy consumption required for cleaning and sterilization processes.

In addition to the liquid and solid waste produced, there is a large amount of carbon dioxide that will be released. The major source for this CO_2 are from the vented bioreactors, which release the gases unused by the cells. Because air is sparged in, the cells take up the oxygen for growth and CO_2 is released. The amount CO_2 released is calculated in Appendix E. Using Sanofi as an example pharmaceutical manufacturing company, their CO_2 emissions were used as a basis for comparison. It was calculated that this process produces 4.1 million kg of CO_2 annually, which is approximately percent of their 455 million kg produced in their company annually. This means that this process produces approximately 6,400 kg CO_2 per kg of mAb produced, using a four month time span to produce 100 kg. [35]

22.2 FDA Regulations

The U.S Food and Drug Administration (FDA) regulates almost every facet of prescription drugs, including testing, manufacturing, labeling, advertising, marketing, efficacy, and safety. The Center for Drug Evaluation and Research (CDER) is the main player in the drug development and approval process, and has different requirements for the three main drug product types: new drugs, generic drugs, and over-the-counter drugs.

Typically, once a promising compound is identified for developments, researchers conduct experiments to gather information on the metabolism, mechanisms of action, optimal dosage and administration, side-effects, biological variation, interactions, and efficacy. Before testing the drug in people, researchers must perform either *in vivo* or *in vitro* toxicity research, following FDA defined good laboratory practices (GLP), which set the minimum basic requirements for study conduct, personnel, facilities, equipment, written protocols, operating procedures, study reports, and quality assurance. The next step is to submit an Investigational New Drug (IND) application to CDER. Thirty days after the submission, clinical research phase trials may begin.[36]

The purpose of the Phase 1 trial is to test the safety and dosage of the drug in 20-100 healthy volunteers or people with the disease/condition. Approximately 70% of all drugs move on to Phase 2, in which up to several hundred participants with the disease and tested for upto two years for drug efficacy and side effects. This phase has a 33% passing rate. The Phase 3 study tests for efficacy and monitors adverse reactions for 1-4 years in 300-3,000 volunteers with

the disease or condition. The final Phase 4 is another safety and efficacy trial for several thousand volunteer patients.

If early evidence is positive, a New Drug Application (NDA) may be submitted to demonstrate that a drug is safe and effective for its intended use in the population studied. The review team then has 6 to 10 months to approve the drug. The approval process involves a project manager, medical officer, statistician, pharmacologist, pharmakineticist, chemist, and microbiologist. Each member reviews the relevant sections of the application, while FDA inspectors travel to the clinical study sites to conduct a routine inspection. The project manager then assembles an "action package" presenting the review team's recommendation, and a senior FDA official makes a decision. The time and money involved in these steps has all been factored into the on-patent economic framework.

The FDA continues to stay involved and performs routine inspections of the manufacturing facilities and performs post-market drug safety monitoring. Manufacturers are required to comply with the Current Good Manufacturing Practice (CGMP) regulations, which contain minimum requirements for the methods, facilities, and controls used in manufacturing, processing and packing of a drug product.[37] To meet these requirements, the staff will be well-trained and operators will monitor various quality checkpoints throughout the process. The use of disposable equipment enhances sterility by preventing cross-contamination.

23. Conclusions and Recommendations

Based on the design exercises and economic analyses, it is recommended that the Small Production Bioreactor Design be implemented for the Ocrevus production project. This scheme, which makes use of disposable single-use bioreactors and staggers processes into small volume batches, is more cost effective both from a capital and operating cost perspective. It is also the preferred choice from an engineering perspective, as it is more flexible in terms of production scaling, it is easier to control operating conditions in smaller volume tanks, and there is reduced risk associated with a faulty batch.

While the sales forecasts are subject to error, it can be concluded that a 15% IRR can be achieved with both an off-patent and on-patent product. For an off-patent sales price of $35,000 per annual treatment, a 15% IRR can be achieved by 2024 even if sales are only 50% of the projected number. For an on-patent sales price of $65,000, a 15% IRR can be achieved by 2022 under similar sales projections. Therefore, it is recommended that the off-patent drug be priced at $35,000 and the on-patent drug at $65,000 per 1200 mg annual treatment. These prices will ensure a 15% IRR within 6 years of production launch even if sales are much lower than forecasted.

If a quicker return is desired, or if the market calls for the sales price to be lower than this, the incurred costs can be reduced by choosing less specialized operating equipment. Many of the reactors and processing units selected for this design are top-of-the-line and make use of sophisticated control units. By employing more traditional controls and choosing generic equipment manufacturers, many of these capital and operating costs may be reduced.

24. Acknowledgements

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Appendix A - Cryogenic Recovery of the CHO Cells

The CHO cells will be stored in a cryogenic freezing tank, and must be recovered before the start of the inoculum preparation steps, which is the first step in mAb production and processing. The protocol for recovering CHO cells are as follows.[44]

1. The frozen 1mL vial of CHO cells must be removed from the cryogenic storage vessel and thawed to room temperature
2. Fresh ActiPro growth medium, which contains 2.8 g/L of sodium bicarbonate, should be added to a 15mL conical tube along with the thawed cells..
3. The cells should be centrifuged at 1,000 rpm for 5 minutes. After centrifugation, the cells should be in pellet form at the bottom of the conical tube.
4. Excess culture media should be suctioned from the conical tube without suctioning up the cells, and the cells should be resuspended in 1 mL of fresh media.
5. After counting the cells with a hemocytometer, the cells should be re-inoculated in fresh ActiPro growth medium at a density of $3x10^6$ cells/mL in a T-75 cell culture flask.
6. The flask containing the cell culture should be incubated at 36.5°C and 7.5% CO_2 for 3 days.
7. The cells should be passaged according to CHO specific protocols, but follow general steps of: media wash to remove dead cells, trypsin incubation for cell detachment from the culture surface, trypsin neutralization and centrifugation, and counting for resuspension at a density of $3x10^6$ cells/mL in a T-75 cell culture flask.
8. The cells should be passaged as in Step 7 at least 2 times before transferring cells to inoculum preparation steps.
9. Just before seeding into the inoculum preparation steps, the cells should be counted for resuspension at a density of $3x10^5$cells/mL in 30 mL of fresh ActiPro growth media.

Appendix B - Growth Media and Feed Supplement Reconstitution

The media used in the upstream production process will be purchased as a powder. Before being added to the bioreactors, it needs to be reconstituted with WFI, as shown in the media prep trains in Section 12. The following protocols will be used.

ActiPro Medium Reconstitution Protocol[38]

1. Fill a clean mixing vessel to 96% of the final volume with high-quality purified water, such as WFI, at ambient temperature (18°C to 25°C) and start mixing.
2. Add 22.36 g/L ActiPro powder slowly to the vessel, avoiding formation of clumps. Mix until no clumps of powder remain. The solution will remain cloudy in this step, but should be clear of any clumps or dry powder residues.
3. Slowly add 6.5mL/L of a 5 N NaOH solution or 3.25 mL/L of a 10 N NaOH solution and mix until solution is clear.
4. Add 1.8g/L sodium bicarbonate into the vessel and mix until dissolved.
5. Adjust the pH to between 6.90 and 7.35 by dropwise addition of 5 N or 10 N NaOh or HCl. After adjusting, continue mixing for an additional 20 minutes to ensure that all components are completely dissolved.
6. Adjust to the final volume with WFI and mix for an additional 10 minutes.
7. Measure and record the final pH and osmolality. The expected pH is 6.90 and 7.55 and the expected osmolality is 270 to 330 mOsmol/kg.
8. Sterilize immediately by membrane filtration. Use a low-binding filter membrane.
9. Store the reconstituted medium protected from light at 2°C to 8°C until use.

CellBoost 7a Powder Supplement Reconstitution[39]

1. Fill a clean mixing vessel to 80% of the final volume with WFI at ambient temperature and start stirring.
2. Add 181.04 g/L CellBoost 7a powder slowly to the vessel, avoiding formation of clumps. Mix for 30 minutes. The solution will remain cloudy in this step, but should be clear of any clumps or dry powder residues.
3. Slowly add 18.6 mL/L of a 5 N NaOH solution or 9.3 mL/L of a 10 N NaOH solution and mix for 60 minutes.

4. Adjust the pH to between 6.60 and 6.80 by dropwise addition of 5 or 10 N NaOH or HCl. After adjusting, continue stirring for an additional 60 minutes to ensure that all components are completely dissolved.
5. Adjust to the final volume with high-quality purified water, such as WFI, and stir for an additional 10 minutes.
6. Measure and record the final pH and osmolality. The expected pH is 6.60 and 6.80 and the expected osmolality is 247 to 303 mOsmol/kg.
7. Sterilize immediately by membrane filtration. Use a low-binding filter membrane type.
8. Store the reconstituted supplement protected from light at 2°C to 8°C until use.

CellBoost 7b Powder Supplement Reconstitution[39]

1. Fill a clean mixing vessel to 80% of the final volume with WFI at ambient temperature and start stirring.
2. Add 94.6 g/L CellBoost 7b powder slowly to the vessel, avoiding formation of clumps. Mix for 30 minutes. The solution will remain cloudy in this step, but should be clear of any clumps or dry powder residues.
3. Slowly add 160.5 mL/L of a 5 N NaOH solution or 80.25 mL/L of a 10 N NaOH solution and mix for 60 minutes.
4. Adjust the pH to between 11.0 and 11.4 by dropwise addition of 5 or 10 N NaOH or HCl. After adjusting, continue stirring for an additional 60 minutes to ensure that all components are completely dissolved.
5. Adjust to the final volume with high-quality purified water, such as WFI, and stir for an additional 10 minutes.
6. Measure and record the final pH and osmolality. The expected pH is 11.0 and 11.4 and the expected osmolality is 218 to 266 mOsmol/kg.
7. Sterilize immediately by membrane filtration. Use a low-binding filter membrane type.
8. Store the reconstituted supplement protected from light at 2°C to 8°C until use.

Appendix C - Clean-in-Place (CIP) & Steam-in-Place (SIP) Protocol

Clean-in-Place Protocol[40]

The Clean-in-place (CIP) process typically involves three cycles after draining the process tank, which can be accomplished during harvest or transfer of the cells.

1. Initially rinse the tank using room temperature, or warm, water for injection (WFI) using a volume proportioned to the inner surface area of the vessel at a flow rate sufficient to forcefully-impinge on the vessel surface to flush the easy-to-remove contents/debris.
2. Clean/wash using heated caustic solution at about a 3 to 8 wt% sodium hydroxide aqueous solution, at a flow rate sufficient to forcefully-impinge on the vessel surface. This solution may me heated to 85°C. The wash volume used may equal the rinse volume used in Step 1.
3. Wash with WFI for a final rinse. The totalized final rinse volume used may equal the rinse volume used in Step 1.

Steam-in-place Protocol[41]

Once the CIP cycle is complete it will be followed by a Sterilize (or Steam) In Place (SIP) step. This involves flowing steam into and through the vessel and all process connections that require thermal sterilization, such as transfer lines, vent lines, and valves. Once all surfaces are brought to greater than 121°C, the system is held at that temperature for more than 15 minutes, often 30 to 60 minutes. Once the SIP time period has elapsed, the steam flow is stopped, and sterile air is admitted into the tank to displace the steam and to maintain a slight positive pressure to ensure no-entry of native contamination. Often live steam will continue to be supplied to lines connected to sterile, process vessels, with closed, isolation valves used to prevent additional steam from entering the sterile vessel. Steam traps are connected to the low-points of these lines, served with live steam, to provide an exit point for steam condensate. To estimate the amount of steam needed for each piece of equipment, an estimate is needed of: the volume of steam needed to fill the vessel and all related pipeline connections plus the steam needed to bring the temperature of the process equipment mass from its starting temperature to the SIP/sterilization temperature. Manufacturing facilities often have on-

site fossil-fuel powered boilers; however, if lacking this an electrically-powered steam generator (often significantly smaller than gas or oil fired, will serve the purpose if the peak steam usage rate can be met.

Appendix D - Oxygen Transfer and Gas Sparging

Oxygen mass transfer and gas sparging rates are critical parameters for cell survival and high product formation in the upstream cell bioreactions. Oxygen (O_2) mass transfer was calculated based on a desired setpoint of 40% dissolved O_2 and a given requirement of 0.19 pmol of O_2 per cell per hour. Using Equation D.1, the oxygen uptake rate by the cells was calculated.

$$OUR = qO_2 \times [Cells]_{max} \times MW_{O2} \quad \text{(D.1)}$$

where, OUR = oxygen uptake rate [g/L/h]
qO_2 = oxygen requirement [mol/cell/h]
$[Cells]_{max}$ = maximum cell concentration in the reactor [cells/L]
MW_{O2} = molecular weight of oxygen [g/mol]

Then, assuming the oxygen uptake rate was equivalent to the oxygen transfer rate (OTR), an oxygen mass transfer coefficient was calculated using Equation D.2

$$OUR = OTR = kL_a \times C^*_{O2} \times (1 - DO) \quad \text{(D.2)}$$

where, OTR = oxygen transfer rate [g/L/h]
kL_a = oxygen mass transfer coefficient [h^{-1}]
C^*_{O2} = solubility of O_2 in water at 1 atm, 36.5°C [g/L]
DO = setpoint for dissolved oxygen in water

Using the calculated oxygen mass transfer coefficient, which should have a value between 12 and 15 h^{-1}, the Van't Riet equation shown in Equation D.3 was applied to find the superficial gas velocity assuming the total specific energy dissipation rate in the bioreactor was 55 W/m^3, or 0.055 W/kg, assuming water is the main volumetric component in the bioreactor. The total specific energy dissipation rate includes both the impeller and gas sparging operations.[42]

$$kL_a = A(\varepsilon_T)^{\alpha}(u_s)^{\beta} \quad \text{(D.3)}$$

where, A = constant, coalesced system
α, β = constants, coalesced system
ε_T = total specific energy dissipation rate [W/kg]
u_s = superficial gas velocity [m/s]

By multiplying the newly calculated superficial gas velocity by the cross-sectional area of the tank, the required sparged flow rate of oxygen for adequate cell growth can be evaluated. Note that the cross-sectional area of the tanks were calculated based on the assumption of

cylindrical geometry with a height to diameter ratio of 2:1. The relevant equations for these calculations can be found in Equations D.4 and D.5.

$$Q_{O2} = u_s \times CSA \times 1000 \quad \text{(D.4)}$$

$$Q_{air} = \frac{Q_{O2} \times \rho_{O2} \times MW_{O2} \times R \times T}{0.21 \times P} \quad \text{(D.5)}$$

$$Q_{vvm,air} = \frac{Q_{air} \times 60}{V_{tank}}$$

where, Q_{O2} = required flow rate of sparged oxygen [L/h]
CSA = cross-sectional area of a cylindrical tank [m^2]
ρ_{O2} = density of O_2 at 1 atm, 36.5°C [g/L]
R = gas constant [J/mol K]
T = temperature of bioreactor [K]
P = pressure of bioreactor [Pa]
Q_{air} = required flow rate of sparged air [L/h]
$Q_{vvm, air}$ = required flow rate of sparged air [vvm, volume of air sparged under standard conditions per volume of liquid per minute]
V_{tank} = volume of the bioreactor [L]

ε_T = total specific energy dissipation rate [W/kg]
u_s = superficial gas velocity [m/s]

Because the solubility of oxygen in water at atmospheric pressure and 36.5°C is so low at a value of 0.00678 mg/L, it is not accurate to assume 100% of the sparged air will be taken up by the cells. Therefore, a conservative estimate of 30% of the sparged air was assumed to be taken up by the cells as oxygen, with the remaining gases filling the headspace and eventually being vented.

All gas sparging rates should be below values of 0.05 vvm to reduce foaming and prevent formation of large bubbles that will be toxic to the cells upon dissipation.[42]

All values for known variables, along with the calculated air sparging rates for larger bioreactor volumes are listed below in Table D.

Table D. Oxygen mass transfer rate and gas flowrates for large volume bioreactors

Known Variables		
qO_2	(mol/cell/h)	0.19
$[Cells]_{max}$	(cells/L)	$9x10^3$
MW_{O2}	(g/mol)	32
C^*_{O2}	(g/L)	0.00678
DO		0.4
A		0.026
α		0.4
β		0.5
ε_T	(W/kg)	0.055
CSA, H/D = 2	(m^2)	6.80
ρ_{O2}, 1 atm, 36.5˚C	(g/L)	1.26
MW_{O2}	(g/mol)	32
R	(J/mol K)	8.31
T	(K)	310
P	(Pa)	200,000
V_{tank}	(L)	20,000
Tank Size	**Air sparging rate [vvm], assuming 30% uptake**	
500 L	0.0423	
2,000 L	0.0211	
20,000 L	0.00981	

Appendix E - Exhaust Venting Rates

Because only 30% of sparged air is taken up by the cells, this leaves 70% of the sparged air to fill the remaining headspace and eventually to be released into the atmosphere through the exhaust vents in each of the bioreactors. In addition, to O_2 and N_2, CO_2 must also be stripped from the culture solution and vented from the bioreactors. Cells produce CO_2 as a result of glucose uptake and use as energy, however CO_2 concentration is a highly controlled parameter that acutely affects cell growth and product quality. It can also displace oxygen as the main gas dissolved in the culture media, which limits further the amount of oxygen available for cellular uptake. The molar ratio of O_2 uptake to CO_2 production by the cells was assumed to be 1, and from this the amount of CO_2 that needs to be stripped and vented can be calculated. All values for known variables, along with the calculated CO_2, O_2, and N_2 venting rates for larger bioreactor volumes are listed below in Table E.

Table E. Venting rates for Oxygen, Nitrogen, and Carbon Dioxide in large volume bioreactors

Known Variables			
ρ_{O2}, 1 atm, 36.5˚C		(g/L)	1.26
ρ_{N2}, 1 atm, 36.5˚C		(g/L)	1.09
ρ_{CO2}, 1 atm, 36.5˚C		(g/L)	1.72
qCO_2		(mol/cell/h)	$0.19x10^{-12}$
Tank Size	**CO_2 venting [kg/h]**	**O_2 venting [kg/h]**	**N_2 venting [kg/h]**
500 L	0.000026	0.116	0.38
2,000 L	0.0000685	0.464	1.53
20,000 L	1.02	2.15	7.09

Appendix F - Economics

F.1 Investment Summary

Large Production Bioreactor Scheme:

Installed Equipment Costs:			
Total Direct Materials and Labor Costs			$23,169,681.75
Miscellaneous Installation Costs			
Material and Labor G&A Overhead and Contractor Fees			
Contractor Engineering Costs			
Indirect Costs			
Total:			**$23,169,681.75**
Direct Permanent Investment			
Cost of Site Preparations:	5.00%	of Total Bare Module Costs	$1,158,484.09
Cost of Service Facilities:	5.00%	of Total Bare Module Costs	$1,158,484.09
Allocated Costs for utility plants and related facilities:			
Direct Permanent Investment			**$25,486,650.03**
Total Depreciable Capital			
Cost of Contingencies & Contra	18.00%	of Direct Permanent Investment	**$4,587,597.00**
Total Depreciable Capital			**$30,074,247.03**
Total Permanent Investment			
Cost of Land:	2.00%	of Total Depreciable Capital	$601,484.94
Cost of Royalties:	0		
Cost of Plant Start-Up:	10.00%	of Total Depreciable Capital	$3,007,424.70
Total Permanent Investment - Unadjusted			**$33,683,156.68**
Site Factor			1
Total Permanent Investment			**$33,683,156.68**
Total Capital Investment			
			$3,093,257,946.12

Small Production Bioreactor Scheme:

Installed Equipment Costs:			
Total Direct Materials and Labor Costs			$13,532,731.35
Miscellaneous Installation Costs			
Material and Labor G&A Overhead and Contractor Fees			
Contractor Engineering Costs			
Indirect Costs			
Total:			**$13,532,731.35**
Direct Permanent Investment			
Cost of Site Preparations:	5.00%	of Total Bare Module Costs	$676,636.57
Cost of Service Facilities:	5.00%	of Total Bare Module Costs	$676,636.57
Allocated Costs for utility plants and related facilities:			
Direct Permanent Investment			**$14,886,004.59**
Total Depreciable Capital			
Cost of Contingencies & Contractor Fee:	18.00%	of Direct Permanent Investment	**$2,679,480.83**
Total Depreciable Capital			**$17,565,485.41**
Total Permanent Investment			
Cost of Land:	2.00%	of Total Depreciable Capital	$351,309.71
Cost of Royalties:	0		
Cost of Plant Start-Up:	10.00%	of Total Depreciable Capital	$1,756,548.54
Total Permanent Investment - Unadjusted			**$19,673,343.66**
Site Factor			1
Total Permanent Investment			**$19,673,343.66**
Total Capital Investment			
			$1,951,000,242.2

F.2 Fixed Costs

Large Production Bioreactor Scheme:

				Expense per BATCH	Annual Expense
OPERATIONS					
	Operators per	Hourly Wage	Hours per BATCH		
Direct Wages and Benefits	8	40	720	**$230,400.00**	
Direct Salaries and Benefits	15%	of Direct Wages and Benefits		**$34,560.00**	
Operating Supplied & Services	6%	of Direct Wages and Benefits		**$13,824.00**	
Technical Assistance to Manufacturing:	$60,000.00	per year, per operator per shift			**$480,000.00**
Control Laboratory	$65,000.00	per year, for each Operator per Shift			**$520,000.00**
MAINTENANCE					**$1,278,784.00**
Wages & Benefits	4.50%	of Total Depreciable Capital		$1,353,341.12	**$1,353,341.12**
Salaries & Benefits	25%	of Maintenance Wages and Benefits			**$338,335.28**
Materials & Services	100%	of Maintenance Wages and Benefits			**$1,353,341.12**
Maintenance Overhead	5%	of Maintenance Wages and Benefits			**$67,667.06**
				Total Maintenance	**$3,112,684.57**
OPERATING OVERHEAD					
General Plant Overhead	7.10%	of Maintenance and Operations Wages and Benefits			**$96,087.22**
Mechanical Department Services	2.40%	of Maintenance and Operations Wages and Benefits			**$32,480.19**
Employee Relations Department	5.90%	of Maintenance and Operations Wages and Benefits			**$79,847.13**
Business Services	7.40%	of Maintenance and Operations Wages and Benefits			**$100,147.24**
				Total Op Overhead	**$308,561.77**
PROPERTY TAXES & INSURANCE	2%	of Total Depreciable Capital			**$601,484.94**

Small Production Bioreactor Scheme:

				Expense per BATCH	Annual Expense
OPERATIONS					
	Operators per shift	Hourly Wage	Hours per BATCH		
Direct Wages and Benefits	8	40	720	**$230,400.00**	
Direct Salaries and Benefits	15%	of Direct Wages and Benefits		**$34,560.00**	
Operating Supplied & Services	6%	of Direct Wages and Benefits		**$13,824.00**	
Technical Assistance to Manufacturing:	$60,000.00	per year, per operator per shift			**$480,000.00**
Control Laboratory	$65,000.00	per year, for each Operator per Shift			**$520,000.00**
MAINTENANCE					**$1,278,784.00**
Wages & Benefits	4.50%	of Total Depreciable Capital		$790,446.84	**$790,446.84**
Salaries & Benefits	25%	of Maintenance Wages and Benefits			**$197,611.71**
Materials & Services	100%	of Maintenance Wages and Benefits			**$790,446.84**
Maintenance Overhead	5%	of Maintenance Wages and Benefits			**$39,522.34**
				Total Maintenance	**$1,818,027.74**
OPERATING OVERHEAD					
General Plant Overhead	7.10%	of Maintenance and Operations Wages and Benefits			**$56,121.73**
Mechanical Department Services	2.40%	of Maintenance and Operations Wages and Benefits			**$18,970.72**
Employee Relations Department	5.90%	of Maintenance and Operations Wages and Benefits			**$46,636.36**
Business Services	7.40%	of Maintenance and Operations Wages and Benefits			**$58,493.07**
				Total Op Overhead	**$180,221.88**
PROPERTY TAXES & INSURANCE	2%	of Total Depreciable Capital			**$351,309.71**

F.3 Working Capital

Large Production Bioreactor Scheme:

WORKING CAPITAL	Cash reserves + Inventory + Accounts Receivable - Accounts Payable					
Accounts Receivable	30 Days	-->	1 Batch of Sales	Annual Sales		**$1,399,476,590.01**
Cash Reserves (excluding Raw Materials)	30 Days	-->	1 Batch	Total Cost of Manufacture	**ops, maint, op overhead, taxes&insurance, util**	
Accounts Payable	30 Days	-->	1 Batch	Annual Feedstock (Cells)	**raw mat, util**	**-$2,547,935.32**
Inventory	4 Days	-->	1 Batch			**$1,399,476,590.01**
Raw Materials	2 Days	-->	1 Batch			**$2,524,922.04**

Small Production Bioreactor Scheme:

WORKING CAPITAL	Cash reserves + Inventory + Accounts Receivable - Accounts Payable					
Accounts Receivable	30 Days	-->	4 batches	Annual Sales		**$1,399,476,590.01**
Cash Reserves (excluding Raw Materials)	30 Days	-->	4 batches	Total Cost of Manufacture	**ops, maint, op overhead, taxes&insurance, util**	
Accounts Payable	30 Days	-->	1 batch	Annual Feedstock (Cells)	**raw mat, util**	**-$751,916.50**
Inventory	4 Days	-->	1 batch			**$349,869,147.50**
Raw Materials	2 Days	-->	1 batch			**$740,985.18**

F.4 Cash Flow Diagrams

F.4.1 Off-Patent Analysis

Large Production Bioreactor Scheme:

CASH FLOW SUMMARY

	P =	$35,000	per 1200 mg
	T =	37%	
	i =	15.00%	

	Year	Treatments	mAB Req'd (kg)	Sales		Batches	Operations	Capital Cost	Working Capital	Variable Costs
Capital Investment	2018					0		$3,094,637,635.66		
Production Year 1	2019	21179.0035	25.4148042	$741,265,122		2	$1,557,568.00		$933,914,443.22	$90,711,992
PY2	2020	51253.18646	61.50382615	$1,793,861,596		3	$1,836,352.00		$700,226,551.94	$214,834,820
PY3	2021	83030.16531	99.63619837	$2,906,055,786		4	$2,115,136.00		$560,097,529.37	$345,841,185
PY4	2022	106278.6116	127.5343339	$3,719,751,406		5	$2,393,920.00		$466,706,085.05	$442,370,964
PY 5	2023	119032.045	142.838454	$4,166,121,574		6	$2,672,704.00		$400,009,869.41	$496,474,654
PY6	2024	133315.8904	159.9790685	$4,666,056,163		7	$2,951,488.00		$0.00	$556,765,034
PY7	2025	135982.2082	163.1786498	$4,759,377,287		7	$2,951,488.00		$0.00	$567,543,624
PY8	2026	138701.8524	166.4422228	$4,854,564,832		7	$2,951,488.00		$0.00	$578,537,785
PY9	2027	141475.8894	169.7710673	$4,951,656,129		7	$2,951,488.00		$0.00	$589,751,830
PY10	2028	144305.4072	173.1664886	$5,050,689,252		7	$2,951,488.00			$601,190,156

	Fixed Costs	Depreciation	Taxes	Net Earnings	Cash Flow	Cumulative NPV at	15.00%
Capital Investment				0	-$3,094,637,635.66	-$3,094,637,635.66	
Production Year 1	$5,580,299.28	$618,927,527.13	$9,636,762	$35,682,066	-$1,517,159,904	-$4,413,907,117.67	
PY2	$5,859,083.28	$990,284,043.41	$215,666,950	$798,550,599	-$891,959,996	-$5,088,357,020.16	
PY3	$6,137,867.28	$594,170,426.05	$725,165,334	$2,685,071,642	$1,530,803,686	-$4,081,828,747.68	
PY4	$6,416,651.28	$356,502,255.63	$1,078,350,768	$3,992,812,303	$3,169,603,962	-$2,269,597,395.09	
PY 5	$6,695,435.28	$356,502,255.63	$1,223,386,215	$4,529,835,445	$3,773,323,320	-$393,688,825.74	
PY6	$6,974,219.28	$178,251,127.81	$1,451,904,339	$5,375,970,122	$5,197,718,994	$1,853,528,531.06	
PY7	$6,974,219.28		$1,548,397,994	$5,733,257,438	$5,733,257,438	$4,008,872,361.29	
PY8	$6,974,219.28		$1,579,549,546	$5,848,602,374	$5,848,602,374	$5,920,790,851.87	
PY9	$6,974,219.28		$1,611,324,129	$5,966,254,209	$5,966,254,209	$7,616,772,664.19	
PY10	$6,974,219.28		$1,643,734,204	$6,086,259,081	$6,086,259,081	$9,121,202,826.48	

CASH FLOW SUMMARY

P =	$35,000	per 1200 mg
T =	37%	
i =	15.00%	

	Year	Treatments	mAB Req'd (kg)	Sales	Batches	Operations	Capital Cost	Working Capital	Variable Costs
Capital Investment	2018				0		$1,951,000,242.22		
Production Year 1	2019	21179.0035	25.4148042	$741,265,122	8	$3,230,272.00		$350,008,643.29	$91,631,454
PY2	2020	51253.18846	61.50382615	$1,793,861,596	10	$3,787,840.00		$720,571,549.53	$214,710,179
PY3	2021	83030.16531	99.63619837	$2,906,055,786	17	$5,739,328.00		$397,686,716.91	$348,432,024
PY4	2022	106278.6116	127.5343339	$3,719,751,406	22	$7,133,248.00		$145,814,731.18	$446,173,450
PY 5	2023	119032.045	142.838454	$4,166,121,574	24	$7,690,816.00		$194,418,231.83	$499,233,038
PY6	2024	133315.8904	159.9790685	$4,666,056,163	27	$8,527,168.00		$62,491,020.69	$559,231,232
PY7	2025	135982.2082	163.1786498	$4,759,377,287	28	$8,805,952.00		$0.00	$570,761,739
PY8	2026	138701.8524	166.4422228	$4,854,564,832	28	$8,805,952.00		$60,336,005.13	$581,755,900
PY9	2027	141475.8894	169.7710673	$4,951,656,129	29	$9,084,736.00		$0.00	$593,721,861
PY10	2028	144305.4072	173.1664886	$5,050,689,252	29	$9,084,736.00			$605,160,187

	Year	Fixed Costs	Depreciation	Taxes	Net Earnings	Cash Flow	Cumulative NPV at	15.00%
Capital Investment	2018			0	0	-$1,951,000,242.	-$1,951,000,242.22	
Production Year 1	2019	$5,579,831.33	$390,200,048.44	$93,925,902	$347,779,691	-$392,429,001	-$2,292,242,851.68	
PY2	2020	$6,137,399.33	$624,320,077.51	$351,016,758	$1,299,710,698	-$45,180,929	-$2,326,406,125.28	
PY3	2021	$8,088,887.33	$374,592,046.51	$804,728,846	$2,979,671,675	$2,207,392,911	-$875,009,454.87	
PY4	2022	$9,482,807.33	$224,755,227.90	$1,124,555,770	$4,163,895,691	$3,793,325,731	$1,293,836,843.70	
PY 5	2023	$10,040,375.33	$224,755,227.90	$1,269,874,385	$4,701,967,319	$4,282,793,859	$3,423,142,312.43	
PY6	2024	$10,876,727.33	$112,377,613.95	$1,473,921,118	$5,457,491,708	$5,282,623,073	$5,706,966,045.78	
PY7	2025	$11,155,511.33		$1,545,660,214	$5,723,120,250	$5,723,120,250	$7,858,498,931.78	
PY8	2026	$11,155,511.33		$1,576,811,766	$5,838,465,187	$5,778,129,181	$9,747,379,610.71	
PY9	2027	$11,434,295.33		$1,608,204,990	$5,954,704,962	$5,954,704,962	$11,440,078,406.19	
PY10	2028	$11,434,295.33		$1,640,615,065	$6,074,709,834	$6,074,709,834	$12,941,653,771.22	

F.2 On-Patent Analysis

Large Production Bioreactor Scheme:

P =	$65,000 per 1200 mg
T =	37%
i =	15.00%

CASH FLOW SUMMARY

	Year	Treatments	mAB Req'd (kg)	Sales	Batches	Operations	Capital Cost	Working Capital	Variable Costs
Patent	2008								
	2009								
	2010								
	2011								
Clinical Trials Start	2012								
	2013								
	2014								
	2015								
	2016								
	2017								
Capital Investment	2018				0		$3,094,637,635.66		
Production Year 1	2019	21179.0035	25.4148042	$1,376,635,227	2	$1,557,568.00		$933,914,443.22	$164,097,239
PY2	2020	51253.18846	61.50382615	$3,331,457,250	3	$1,836,352.00		$700,226,551.94	$392,427,118
PY3	2021	83030.16531	99.63619837	$5,396,960,745	4	$2,115,136.00		$560,097,529.37	$633,540,707
PY4	2022	106278.6116	127.5343339	$6,908,109,754	5	$2,393,920.00		$466,706,085.05	$810,626,353
PY 5	2023	119032.045	142.838454	$7,737,082,924	6	$2,672,704.00		$400,009,869.41	$908,920,690
PY6	2024	133315.8904	159.9790685	$8,665,532,875	7	$2,951,488.00		$0.00	$1,018,704,594
PY7	2025	135982.2082	163.1786498	$8,838,843,532	7	$2,951,488.00		$0.00	$1,038,721,975
PY8	2026	138701.8524	166.4422228	$9,015,620,403	7	$2,951,488.00		$0.00	$1,059,139,704
PY9	2027	141475.8894	169.7710673	$9,195,932,811	7	$2,951,488.00		$0.00	$1,079,965,787
PY10	2028	144305.4072	173.1664886	$9,379,851,467	7	$2,951,488.00		-$3,060,954,478.99	$1,101,208,392

	Year	Fixed Costs	Depreciation	Taxes	Net Earnings	Cash Flow	Cumulative NPV at	15.00%
Patent	2008	$197,120,000.00				-$197,120,000.00	-$197,120,000.00	
	2009	$197,120,000.00			0	-$197,120,000.00	-$368,528,695.65	
	2010	$197,120,000.00			0	-$197,120,000.00	-$517,579,735.35	
	2011	$197,120,000.00			0	-$197,120,000.00	-$647,189,335.09	
Clinical Trials Start	2012	$253,074,285.71			0	-$253,074,285.71	-$791,885,379.32	
	2013	$253,074,285.71			0	-$253,074,285.71	-$917,708,026.48	
	2014	$253,074,285.71			0	-$253,074,285.71	-$1,027,119,024.01	
	2015	$253,074,285.71			0	-$253,074,285.71	-$1,122,259,021.86	
	2016	$253,074,285.71			0	-$253,074,285.71	-$1,204,989,454.78	
	2017	$253,074,285.71			0	-$253,074,285.71	-$1,276,928,961.66	
Capital Investment	2018			0	0	-$3,094,637,635.66	-$2,041,876,056.18	
Production Year 1	2019	$5,580,299.28	$618,927,527.13	$217,571,160	$805,601,321	-$747,240,649	-$2,202,490,369.46	
PY2	2020	$5,859,083.28	$990,284,043.41	$718,868,192	$2,661,755,197	$971,244,601	-$2,020,957,808.87	
PY3	2021	$6,137,867.28	$594,170,426.05	$1,540,351,345	$5,703,463,090	$4,549,195,134	-$1,281,586,419.13	
PY4	2022	$6,416,651.28	$356,502,255.63	$2,121,788,863	$7,856,353,356	$7,033,145,015	-$287,601,472.67	
PY 5	2023	$6,695,435.28	$356,502,255.63	$2,392,036,881	$8,857,001,425	$8,100,489,300	$707,903,989.71	
PY6	2024	$6,974,219.28	$178,251,127.81	$2,760,793,085	$10,222,396,019	$10,044,144,891	$1,781,269,220.77	
PY7	2025	$6,974,219.28		$2,883,464,515	$10,676,611,853	$10,676,611,853	$2,773,402,844.51	
PY8	2026	$6,974,219.28		$2,941,317,398	$10,890,823,878	$10,890,823,878	$3,653,437,162.84	
PY9	2027	$6,974,219.28		$3,000,327,338	$11,109,320,143	$11,109,320,143	$4,434,037,106.34	
PY10	2028	$6,974,219.28		$3,060,517,477	$11,332,186,333	$14,393,140,812	$5,313,462,024.79	

Small Production Bioreactor Scheme:

CASH FLOW SUMMARY

P =	$65,000 per 1200 mg
T =	37%
i =	15.00%

	Year	Treatments	mAB Req'd (kg)	Sales	Batches	Operations	Capital Cost	Working Capital	Variable Costs
Patent	2008						$197,120,000.00		
	2009						$197,120,000.00		
	2010						$197,120,000.00		
	2011						$197,120,000.00		
Clinical Trials Start	2012						$253,074,285.71		
	2013						$253,074,285.71		
	2014						$253,074,285.71		
	2015						$253,074,285.71		
	2016						$253,074,285.71		
	2017						$253,074,285.71		
Capital Investment	2018				0		$1,951,000,242.22		
Production Year 1	2019	21179.0035	25.4148042	$1,376,635,227	8	$3,230,272.00		$350,008,643.29	$165,016,701
PY2	2020	51253.18846	61.50382615	$3,331,457,250	10	$3,787,840.00		$720,571,549.53	$392,302,477
PY3	2021	83030.16531	99.63619837	$5,396,960,745	17	$5,739,328.00		$397,686,716.91	$636,131,547
PY4	2022	106278.6116	127.5343339	$6,908,109,754	22	$7,133,248.00		$145,814,731.18	$814,428,840
PY 5	2023	119032.045	142.838454	$7,737,082,924	24	$7,690,816.00		$194,418,231.83	$911,679,074
PY6	2024	133315.8904	159.9790685	$8,665,532,875	27	$8,527,168.00		$62,491,020.69	$1,021,170,793
PY7	2025	135982.2082	163.1786498	$8,838,843,532	28	$8,805,952.00		$0.00	$1,041,940,090
PY8	2026	138701.8524	166.4422228	$9,015,620,403	28	$8,805,952.00		$60,336,005.13	$1,062,357,819
PY9	2027	141475.8894	169.7710673	$9,195,932,811	29	$9,084,736.00		$0.00	$1,083,935,818
PY10	2028	144305.4072	173.1664886	$9,379,851,467	29	$9,084,736.00		-$1,931,326,898.56	$1,105,178,423

	Year	Fixed Costs	Depreciation	Taxable Income	Taxes	Net Earnings	Cash Flow	Cumulative NPV at	15.00%
Patent	2008						-$197,120,000.00	-$197,120,000.00	
	2009						0 -$197,120,000.00	-$368,528,695.65	
	2010						0 -$197,120,000.00	-$517,579,735.35	
	2011						0 -$197,120,000.00	-$647,189,335.09	
Clinical Trials Start	2012						0 -$253,074,285.71	-$791,885,379.32	
	2013						0 -$253,074,285.71	-$917,708,026.48	
	2014						0 -$253,074,285.71	-$1,027,119,024.01	
	2015						0 -$253,074,285.71	-$1,122,259,021.86	
	2016						0 -$253,074,285.71	-$1,204,989,454.78	
	2017						0 -$253,074,285.71	-$1,276,928,961.66	
Capital Investment	2018				0		0 -$1,951,000,242.2	-$1,759,186,383.18	
Production Year 1	2019	$5,579,831.33	$390,200,048.44	$815,838,647	$301,860,299	$1,117,698,946	$377,490,254	-$1,678,047,411.38	
PY2	2020	$6,137,399.33	$624,320,077.51	$2,308,697,296	$854,217,999	$3,162,915,295	$1,818,023,668	-$1,338,245,788.59	
PY3	2021	$8,088,887.33	$374,592,046.51	$4,378,148,265	$1,619,914,858	$5,998,063,122	$5,225,784,359	-$488,909,734.65	
PY4	2022	$9,482,807.33	$224,755,227.90	$5,859,442,879	$2,167,993,865	$8,027,436,744	$7,656,866,785	$593,224,972.43	
PY 5	2023	$10,040,375.33	$224,755,227.90	$6,590,608,247	$2,438,525,051	$9,029,133,298	$8,609,959,839	$1,651,341,554.44	
PY6	2024	$10,876,727.33	$112,377,613.95	$7,521,107,741	$2,782,809,864	$10,303,917,605	$10,129,048,971	$2,733,780,040.40	
PY7	2025	$11,155,511.33		$7,785,747,931	$2,880,726,734	$10,666,474,665	$10,666,474,665	$3,724,971,657.01	
PY8	2026	$11,155,511.33		$7,942,107,073	$2,938,579,617	$10,880,686,690	$10,820,350,685	$4,599,311,380.64	
PY9	2027	$11,434,295.33		$8,100,562,698	$2,997,208,198	$11,097,770,896	$11,097,770,896	$5,379,099,812.59	
PY10	2028	$11,434,295.33		$8,263,238,749	$3,057,398,337	$11,320,637,086	$13,251,963,985	$6,188,798,508.56	

ReadyToProcess™

WAVE 25 rocking bioreactor system

The single-use ReadyToProcess WAVE™ 25 rocking bioreactor system is a reliable and intuitive cell culture system for working volumes up to 25 L (Fig 1). The system is based on a well-known rocking technology that provides mixing and aeration to the culture, which is maintained in an inflated, disposable Cellbag™ bioreactor cultivation chamber.

With ReadyToProcess WAVE 25, the rocking technology is enhanced with features such as advanced sensors and intelligent control strategies. System operation is easily managed via the intuitive and user-friendly UNICORN™ system control software. The system is designed for fast installation and convenient handling, and it delivers a reliable and accurate performance suitable for research, process development, and manufacturing operations.

ReadyToProcess WAVE 25 offers the following benefits:

- Robust and reliable performance
- Intelligent and accurate process control
- Designed for ease of use
- Flexible operations with possibility of use in single or dual culture mode
- Suitable for manufacturing in a regulated environment

Fig 1. ReadyToProcess WAVE 25 bioreactor system.

System benefits

Robust and reliable performance

ReadyToProcess WAVE 25 is designed to make hardware, consumables, and software work together in an integrated manner. The system has been tested in real applications for reliable performance. To decrease the risk for data losses, the system comprises two, mirrored, solid-state drives for data storage.

Intelligent and accurate process control

The system is equipped with advanced sensors and automated controllers for temperature, liquid handling, pH, and dissolved oxygen (DO). The system dynamics have been methodically characterized and the results used to create a library of predefined control parameters tailored for different cultivation volumes. The system can automatically determine suitable parameters for a run, a feature that facilitates fast start-up and enables accurate and stable control.

Easy to use

ReadyToProcess WAVE 25 system is designed for ease of use. Cellbag bioreactor attachment is straightforward and system operation is conveniently managed with the UNICORN software, with menus and process pictures that are easily accessible and interpretable. The harvest operation is facilitated by an innovative tilt function that avoids the need for heavy lifting.

Flexible operations with possibility of use in single or dual culture mode

With ReadyToProcess WAVE 25, one or two cultures can be run at the same time with high control accuracy. When dual mode is used, two cultivations can be run using the same or different bag sizes and/or working volumes. Parameters such as temperature, pH, and DO can be controlled independently in the two Cellbag bioreactors. Separate pump units control liquid addition and/or removal, for example, to enable tailored feeding strategies, base addition, or perfusion in the two parallel cultures.

Suitable for manufacturing in a regulated environment

ReadyToProcess WAVE 25 is designed to meet the demands and standards that are required in a regulated environment. The documentation is extensive and includes material certificates, system specifications, installation and operational qualification (IQ/OQ) protocols, and a detailed user manual. The UNICORN software is suitable for use in a manner that complies with 21 CFR Part 11 and Good Automated Manufacturing Practice (GAMP™) 5.

System overview

ReadyToProcess WAVE 25 system components

The ReadyToProcess WAVE 25 system consists of a rocker, CBCU gas mixers, and pumps, all operated by the UNICORN software installed on a client computer. The rocker is the main unit and is used together with a tray and a disposable Cellbag bioreactor. When operated in dual culture mode, culturing can be performed in two separate Cellbag bioreactors simultaneously, although controlled separately. The rocker has multiple functions, amongst them including temperature control, culture mixing, and weight measurement. The CBCU contains a gas mixer that delivers gas of a defined composition to the culture and is used together with the optical sensors of the Cellbag bioreactor for online control of culture pH and DO. Liquid is delivered accurately to the culture by ReadyToProcess Pump 25. The pump unit has a flow range covering multiple applications, from additions of feed and base to perfusion culturing. Up to two CBCU gas mixers and up to three pump units can be connected to ReadyToProcess WAVE 25. An overview of the ReadyToProcess WAVE 25 system is shown in Figure 2. The individual components are described in detail below.

System setup and integration of subunits

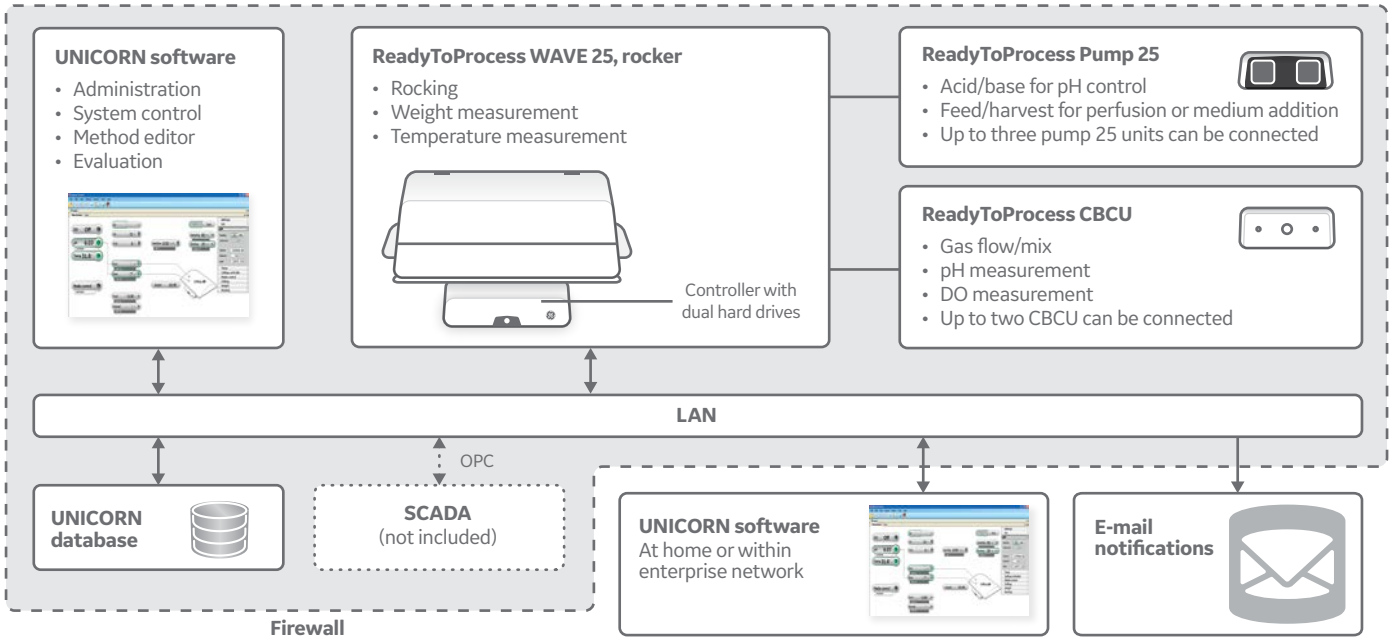

Fig 2. ReadyToProcess WAVE 25 system overview. The System Control module on the client computer is used to start and monitor the cultivation process. One UNICORN client can control up to three ReadyToProcess WAVE 25 systems simultaneously. SCADA = supervisory control and data acquisition, OPC = open platform communications, LAN = local area network.

ReadyToProcess WAVE 25, rocker

The rocker is the main hardware unit of the system and provides mixing through the rocking, reliable temperature measurement from integrated sensors, and accurate weight measurement from integrated load cells. The ergonomic design makes handling convenient and easy. The ability to handle the bioreactor in a tilt position facilitates sampling and harvest (Fig 3). The minimal footprint facilitates placement when space is limited.

(A) (B)

Fig 3. (A) The ergonomic design makes activities such as sampling and harvest convenient and easy. (B) ReadyToProcess WAVE 25 in tilt position.

Trays and lids

Trays are available in three different sizes for culturing of up to 5 L, 10 L, and 25 L, respectively. The trays are easily attached to the rocker when in the tilt position. A snap lock mechanism allows Cellbag bioreactors to be correctly installed and rapidly changed (Fig 4). To protect light-sensitive components of the culture medium and to prolong the life of the optical sensors, lids are available for all tray sizes.

Fig 4. The tray has an easy lock mechanism for convenient and proper attachment of Cellbag bioreactors.

Temperature control

Efficient and evenly distributed heating is provided by the tray heater plate. The temperature control is managed by sensors that are integrated in the rocker base unit to enable reliable temperature measurement and to minimize the need for calibration when changing trays (Fig 5). To minimize the risk for overheating, heating is only enabled when the rocker is in motion. For accurate, stable, and fast temperature control, the heater power output is automatically adjusted based on the Cellbag bioreactor size and content weight. Temperature control in two separate Cellbag bioreactor cultures when using the dual functionality is shown in Figure 6.

Fig 5. Integrated temperature sensors for convenient handling and reliable temperature control.

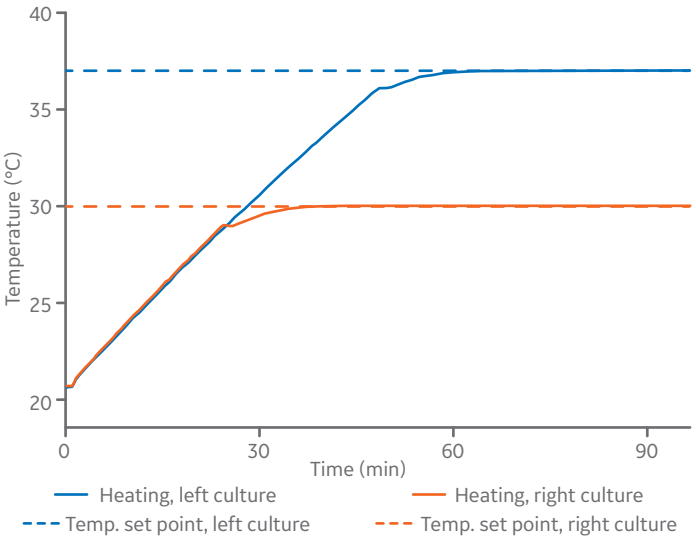

Fig 6. Temperature is accurately controlled independently in two separate 5 L cultures using the dual functionality (ambient temperature 22°C).

Mixing and gas transfer

The adjustable rocking parameters are speed, angle, and motion. The parameter settings, in combination with the cell culture volume, affect the mixing and gas transfer rate in the Cellbag bioreactor. The speed parameter determines the number of rocking cycles per minute, and the angle parameter relates to the tray's degree of tilting at the turning points. The motion parameter determines the acceleration profile. The lowest motion parameter setting, 15%, gives an almost constant speed throughout the rocking cycle. In contrast, the highest setting, 100%, gives a faster speed in the middle of the cycle and slower at the turning points. Whereas oxygen transfer coefficient increases with increasing rocking speed and angle, the rocking motion pattern only has a minor effect on the oxygen transfer rate (Fig 7).

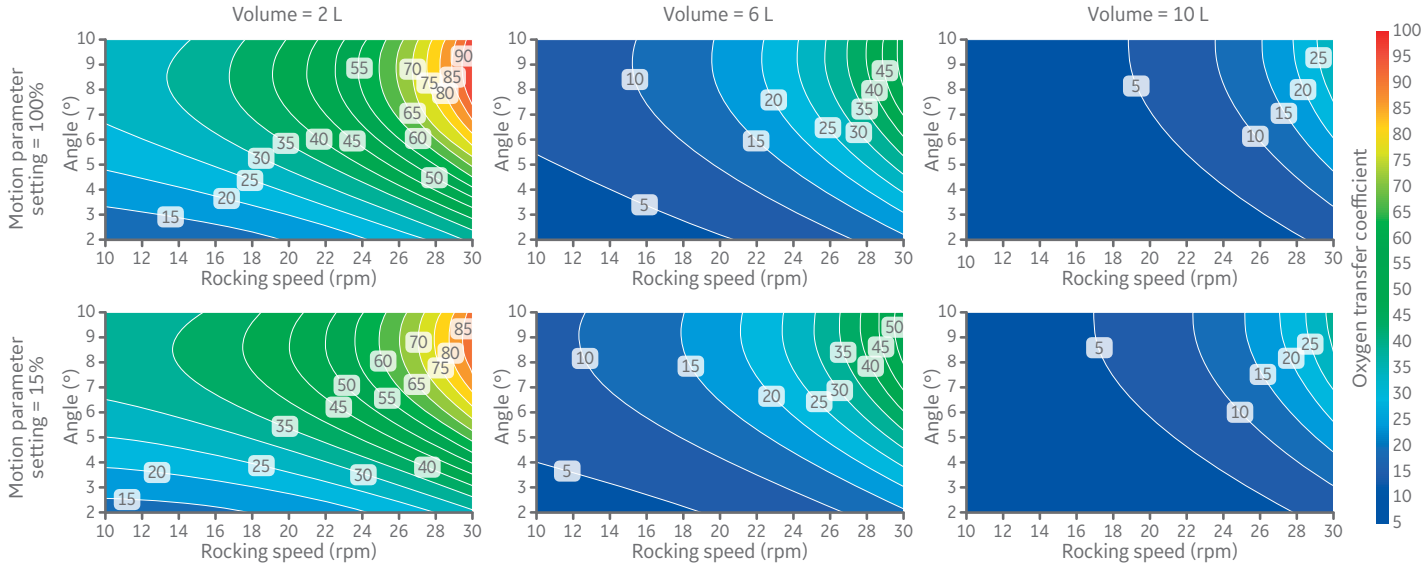

Fig 7. 4D contour plot of the oxygen transfer coefficient at the highest (100%) and lowest (15%) rocking motion parameter settings.

Weight measurement

Load cells integrated in the rocker provide accurate and continuous weight measurement of the culture and eliminate the need for external scales. In dual mode, separate weight measurements are provided for each Cellbag bioreactor. The load cells communicate with the system control function for proper media handling and tailored regulation of pH and temperature. The weight measurement functionality is also used for automatic calibration of the pumps in perfusion cultures. An adjustable foot enables equal weight distribution between the load cells even on nonlevel surfaces, for increased precision of the weight measurement.

Data storage and communication

Data and control parameters from the cell culture run are stored on two independent, mirrored, solid-state drives integrated in the rocker. Thus, once cultivation has been started and data from the instrument modules have been collected, the run can continue without the need for a network connection. The use of two solid-state drives enables culturing without losing any data even if only one drive is functional. After a run, data is stored in a UNICORN database on an external computer. For facilitated integration into a larger manufacturing operation, the rocker also contains software for enabling direct communication with the system via an open platform communication (OPC) link.

ReadyToProcess CBCU

The ReadyToProcess CBCU gas mixer is a compact unit with multiple functions. The unit is primarily used for providing gas to the culture and for monitoring of pH and DO. The unit contains a mass flow controller, sensors for gas pressure and O_2 and CO_2 concentrations, and transmitters for pH and DO (Table 1).

Table 1. ReadyToProcess CBCU gas mixer overview

Feature	Description
CO_2/O_2/air mix controller	Depending on the configuration, air is mixed with CO_2 and/or O_2 according to the set-points. Nitrogen can be used instead of air for maintaining a low oxygen environment for near-anaerobic applications.
Gas flow controller	The gas-mix flow is measured and controlled by a mass flow controller (MFC). A correct volumetric flow is achieved by compensation for CO_2 concentration. Quick filling of gas into the Cellbag bioreactor, enabled by the fast-fill function, significantly reduces start-up time. An alarm will inform the user if pressure sensors detect under or overpressure at the gas inlets or within the Cellbag bioreactor.
pH measurement	The pH is measured with optical pH sensors preinstalled in Cellbag bioreactors of pHOPT type. The sensor is connected to the CBCU via an optical fiber cable.
DO measurement	The DO level is measured with optical DO sensors preinstalled in Cellbag bioreactors of DOOPT type. The sensor is connected to the CBCU via an optical fiber cable.

Three CBCU configurations are available:

- CO_2, O_2, and pH
- CO_2, O_2, and DO
- CO_2, O_2, pH, and DO

The most suitable CBCU configuration will depend on the specific application.

ReadyToProcess Pump 25

The ReadyToProcess Pump 25 is a peristaltic unit incorporating two roller pumps for feed, harvest, and pH control. The pump design makes tubing installation convenient and easy. Tubing sizes from 0.5 mm (1/50") to 4.8 mm (3/16") internal diameter can be used to support flow rates from 0.07 to 100 mL/min. Flow rate is regulated by weight feedback from the scale and is controlled by automatic adjustments of the pump speed. Manual adjustment of the flow rate is also possible.

Up to three pump units with a total of six pump heads can be connected to the rocker. Up to six pump roles can be selected from a set of 12 options (left: acid, base, feed1, feed2, feed3, or harvest; and right: acid, base, feed1, feed2, feed3, or harvest) for the dual mode and seven options (acid, base, feed1, feed2, feed3, feed4, or harvest) for the single mode.

Media handling and perfusion using calibrated pumps

Calibration of pumps can be performed manually or automatically during an ongoing perfusion process. Automatic calibration is possible for flow rates above 3.5 L/d and is easily managed by entering the tubing diameter in the UNICORN control software.

Automated pH control

To minimize fluctuations in pH during adjustments with CO_2/base or acid/base, the flow rate of the acid/base pumps needs to be rigorously controlled. The ReadyToProcess WAVE 25 system uses combined information from the load cells, the current process pH value, the pump tubing diameter, and the acid/base molarity for calculation of the needed flow rate during the run.

Automation of process parameters in pH and DO control

The UNICORN software automatically sets the desired PID (Proportional-integral-derivative) control parameters based on Cellbag bioreactor size and gas flow set-point. The system also adapts the parameters during the run, for optimization to reach a new set-point or to maintain a current set-point.

UNICORN software

UNICORN system control software consists of four modules: *Administration*, *Method editor*, *System control*, and *Evaluation*. A comprehensive help tool is also included.

Administration

The *Administration* module is used to administer all functions of the UNICORN software. Available functions include user and email setup, controlling access to groups and network users, defining and editing system properties, database management, and logging records of usage and activity.

Method editor

Instructions to control a bioreactor run can be defined in a method. The *Method editor* module is used to create, edit, save, and work with methods. An existing method can be changed to simplify the editing process. Individual changes can be saved for later use on systems that have the same instrument and component configuration.

System control

The *System control* module is used to connect to the system as well as to start, view, and control a run (Fig 8). Default parameter values for an instrument can be viewed and edited in the *System settings* dialog before a run is started or during an ongoing run using manual instructions. It is also possible to connect to other systems.

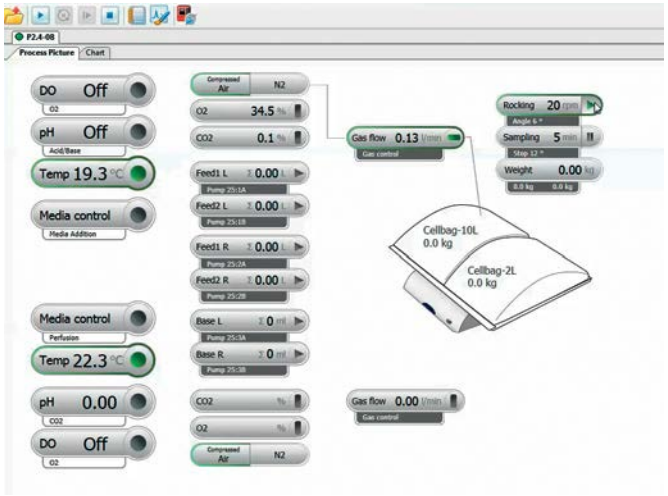

Fig 8. Monitoring and controlling all aspects of the culture is managed through the user-friendly interface.

The user-friendly and intuitive *Process picture* pane enables manual interaction with the system and provides status of the run parameters. Data is shown in the process picture but can also be viewed as curves in the *Charts* tab. Curves and information about the run are saved in a database, which can be opened in the *Evaluation* module. The default view shows the curves most commonly used. The user can customize which curves to display and the color and style of the displayed curves.

Evaluation

In the *Evaluation* module, content of the result files can be viewed, analyzed, and compiled as reports. Reports can be customized, saved, and printed.

Alarms, notifications, and data logging

The UNICORN software allows easy access to all operations, data, and alarm conditions. A dynamic, graphical user interface shows the real-time status of the run, while data are automatically saved. From the UNICORN software, the system is easily configured to trigger an alarm when certain conditions are met. Individual deviation alarms can be set for all essential parameters (heating, gas flow, weight, O_2, CO_2, pH, and DO). The regulation of alarm sensitivity and delay is defined by the user. If such an alarm condition is triggered, the part of the system generating the alarm is highlighted in the graphical user interface and an alarm dialog is displayed. The alarm dialog displays information about the alarm, such as date and time of occurrence, as well as a help text describing the cause of the alarm and how to solve the problem. The system is easily configured to send email notifications of alarms and errors.

Regulatory readiness

The ReadyToProcess WAVE 25 system is suitable for biomanufacturing of regulated products under various Quality Management Systems. The use of UNICORN software in a 21 CFR Part 11 and GAMP 5 compliant manner enables use of the system in a regulated environment. Individual user access permissions can be set and individual users are password-protected. Active processes can be locked to enable unattended operations without the risk of unauthorized interference. All records are stored in a single, unalterable database, including results and

extended run documentation. Additional validation support includes comprehensive documentation on control system validation as well as IQ/OQ services. The IQ/OQ offers proven test procedures, verifying that the equipment has been installed in accordance with system drawings and specifications. The IQ/OQ also assures that the system operates as specified in the design, satisfying functional requirements. The IQ/OQ protocols enable quality assurance and allow regulatory reviewers to verify that all functional testing of the quality critical equipment and components, including the requirements of 21 CFR Part 11, has been performed and documented.

Available validation support documentation includes:

- Detailed description of the development model used for UNICORN software
- 21 CFR Part 11 system assessment in checklist format
- Audit report and 21 CFR Part 11 conclusion on functionality by an external, independent expert

Networking capabilities

UNICORN 7 operates in Windows® 7 and Windows 10 environments, and the network ability allows real-time control from a remote or local computer. Communication is Ethernet-based and each instrument is controlled by a built-in instrument server. One database can be connected to 32 systems, and up to three instruments can be controlled simultaneously from one UNICORN client. Results are saved locally, in the rocker, during the run and then stored on the database server. Because results and instructions are saved locally on the embedded drives, a run can continue even in the event of a network communication failure.

Many users within biopharmaceutical and pharmaceutical operations require automation in seed train and process development. Although UNICORN provides the capability to control standalone WAVE 25 bioreactors, many users of the Emerson DeltaV™ Distributed Control System (DCS) prefer a single interface to monitor and control all unit operations together, including a WAVE 25 bioreactor system.

OPC UaGateway®

As an alternative to UNICORN communication, a WAVE 25 system can also be setup to communicate set points and monitor process values from the DeltaV operator station. To accomplish this, the Open Platform Communications (OPC) UaGateway option that comes with the WAVE 25 system can be used. The OPC UaGateway provides a more streamlined connection for process control and monitoring; it eliminates complexities associated with the Distributed Component Object Model (DCOM)-based configuration.

Fig 9. Setup of the WAVE 25 Bioreactor System on a client PC with DeltaV.

The architecture in Figure 9 shows a system consisting of an embedded personal computer (EPC) on the WAVE 25 system and a Client PC (any Windows system) on DeltaV.

UaGateway is used as data communication tunneller between the WAVE 25 and the DeltaV systems. Two OPC UaGateway instances are required for communication: the first instance is installed on the WAVE 25 system, the second instance goes on the DeltaV OPC server on the user's network. Because two OPC servers do not communicate directly according to the OPC protocol, a third-party data manager or an OPC bridge software needs to be added and configured to allow communication between the two OPC servers.

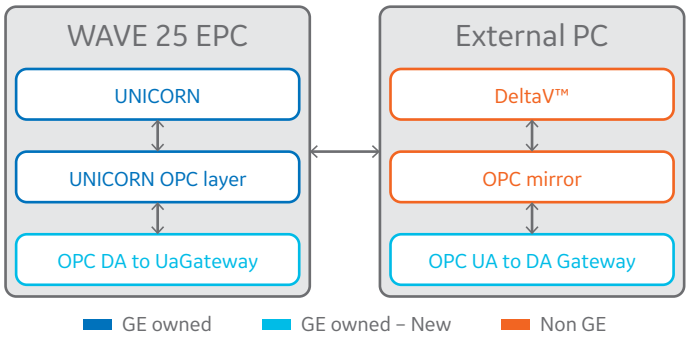

Fig 10. UaGateway architecture.

Please note that UNICORN client license is still required to perform for the system's initial configuration and definition. It is recommended to install UNICORN on the OPC server on the DeltaV network. Please contact your local representative for further information.

Cellbag bioreactors

Presterilized Cellbag bioreactors are single-use bags for the noninvasive mixing of culture medium and cells during cultivation (Fig 11). Cellbag bioreactors require no sterilization or cleaning steps. The disposable bioreactors provide a suitable environment for cell growth while minimizing the cross-contamination risk.

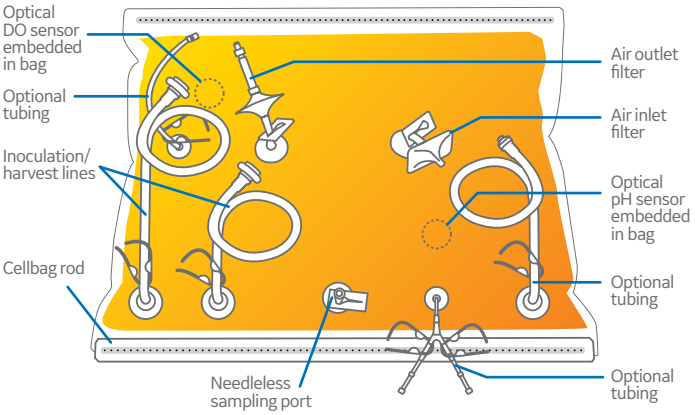

Fig 11. Presentation of typical Cellbag bioreactor fittings.

The bags are manufactured from multilayer, laminated, clear USP Class VI plastics and are easily connected to the full suite of ReadyToProcess cell culture, purification, and fluid handling products. Table 2 shows possible combinations of Cellbag bioreactors and trays when culturing in single or dual mode.

Cellbag bioreactors are available in two films: Bioclear™ 10 and the low-antioxidant Bioclear 11. For more information about Cellbag bioreactors, see data file 28951136.

Table 2. Possible combinations of Cellbag bioreactors and trays when culturing in single or dual mode

Cellbag bioreactor size (L)*	Bioreactor culture volume (L)	Tray	
		Single culture mode	Dual culture mode
2	0.3† to 1	Tray 10, Tray 20	Tray 20
10	0.5 to 5	Tray 10, Tray 20	Tray 20
20	1 to 10	Tray 20	Not applicable
22	1 to 10	Tray 50	Tray 50
50	5 to 25	Tray 50	Not applicable

* All Cellbag bioreactor sizes are available with internal perfusion filter for perfusion cultures and/or can be equipped with single use optical pH (pHOPT) and DO (DOOPT II) sensors.

† Cellbag bioreactors with optical sensors require 300 mL minimal working volume. Depending on application and configuration, it might be possible to cultivate below the recommended minimum volume. However, it is highly recommended to stay above this volume for applications that require high agitation and pH and DO control. The temperature, pH, and DO sensors need to be submerged in liquid throughout the complete rocking cycle to function correctly.

System specifications

System specifications are listed in Table 3.

Table 3. ReadyToProcess WAVE 25 system specifications

General system specifications

Control system	UNICORN 6.3.2 or later version	
Dimensions, W × H × D		
Rocker	404 × 205 × 560 mm	
Tray 10	475 × 60 × 430 mm	
Tray 20	740 × 70 × 480 mm	
Tray 50	800 × 70 × 610 mm	
Lid 10	475 × 230 × 430 mm	
Lid 20	740 × 245 × 480 mm	
Lid 50	800 × 260 × 610 mm	
CBCU	276 × 117 × 360 mm	
Pump 25	275 × 115 × 280 mm	
Weight		
Rocker	24.0 kg	
Tray 10	4.5 kg	
Tray 20	7.3 kg	
Tray 50	9.5 kg	
Lid 10	1.7 kg	
Lid 20	3.3 kg	
Lid 50	3.9 kg	
CBCU	4.8 kg	
Pump 25	3.8 kg	
Power supply	100 to 240 V, ~ 50 to 60 Hz	
Power consumption	1500 VA	
Enclosure protective class	IP 21	
Gas supply (per CBCU)	Normal use	Fast fill
External air supply, 1.0 to 1.5 bar	1.3 L/min	3.5 L/min
External CO_2 supply, 1.0 to 1.5 bar	0.2 L/min	0.5 L/min
External O_2 supply, 1.0 to 1.5 bar	0.7 L/min	1.7 L/min

Environmental aspects

Operating ambient temperature range	15°C to 32°C
Operating humidity range	20% to 80% relative humidity (noncondensing)

ReadyToProcess WAVE 25, rocker

Rocking speed control range[1]	2 to 40 rpm
Rocking angle control range[1]	2° to 12°
Rocking motion control range	15% to 100%
Medium weight control range	0.2 to 25 kg
Scale, absolute accuracy	± (0.050 + 1% of load) kg
Scale, left/right absolute accuracy (dual mode)	± (0.1 + 6% of load) kg
Temperature sensor	Pt100 Class A
Temperature measurement range	2°C to 50°C
Temperature measurement accuracy	± 0.3°C in the range of 15°C to 50°C within ± 5°C from calibration temperature
Temperature control range	(ambient temperature + 5°C) to 40°C
Temperature control accuracy (excl. measurement error)	± 0.2°C
Temperature set point difference (dual mode)	Max. 10°C at ambient temperature (21°C) Set point difference reduced by 1°C for each °C increase in ambient temperature (e.g., at ambient 25°C, max. set point difference is 6°C)

[1] When cultivating in a 50 L Cellbag bioreactor at maximum working volume of 25 L, rocking speed and angle multiplied should not exceed 240 rpm degrees. For example, if the rocking angle is set to 12 degrees, the rocking speed should not be set higher than 20 rpm.

ReadyToProcess CBCU

Gas flow control range	50 to 1000 mL/min
Total gas flow accuracy (reference flow – set point)	± (10 + 3% of read value) mL/min
Fast-fill flow	~ 3 L/min
CO_2 control range	0% to 15% CO_2
CO_2 measurement accuracy at 5% CO_2	± 0.5% CO_2 when mixed only with air/N_2
CO_2 control accuracy (versus set point)	± 0.4% CO_2
O_2 control range	0% to 50% O_2 when mixed with N_2, 21% to 50% O_2 when mixed with air
O_2 measurement accuracy	± (0.6% + 1% of read value) % O_2 within 0% to 50% O_2 when mixed only with air/N_2
O_2 control accuracy (versus set point)	± 0.6% O_2
pH measurement range	pH 4.5 to 8.5
pH control range	pH 6.0 to 8.0
pH measurement accuracy	± 0.05 pH within ± 0.25 pH from offset calibration pH ± 0.1 pH within 0.25 to 0.5 pH from offset calibration
pH control accuracy (versus set point)	± 0.05 pH
DO measurement range	0% to 250% air saturation
DO measurement accuracy	± 5% air saturation (excl. atmospheric pressure variations)
DO control range	0% to 100% air saturation

ReadyToProcess Pump 25

Pump flow rate range	0.1 to 144 L/d (0.07 to 100 mL/min)
Pump flow accuracy	± (0.1 + 5% of read value) mL/min after calibration
Accumulated pumped volume accuracy	± 10% of measured volume
Supported tubing dimensions	i.d. 0.5 to 4.8 mm (1/50" to 3/16") wall thickness: 1.6 mm (1/16")

Applications

ReadyToProcess WAVE 25 is designed for a variety of cell culture applications involving mammalian, insect, and plant cells:

- Batch culture
- Fed-batch culture
- Perfusion culture
- Cultivation of adherent cells

Ordering information

Product	Description	Product code
ReadyToProcess WAVE 25	Rocker	28988000
ReadyToProcess CBCU pH	Gas flow/mix and pH	29044213
ReadyToProcess CBCU DO	Gas flow/mix and DO	29044216
ReadyToProcess CBCU Full	Gas flow/mix, pH, and DO	29044081
ReadyToProcess Pump 25	Pump	29032003
UNICORN 7 WrkStn pure-BP-exp	License	29128116
UNICORN 7 Remote	License	29115426
UNICORN 7 Dry	License	29115427
UNICORN 7 Evaluation Classic	License	29115456
UNICORN 7.0.2 DVD pack	Media (no license)	29195162
OPC DA to UaGateway Converter	Software	29292362
OPC UA to DA Tunneller	Software	29292368
Tray 10	–	29044472
Tray 20	–	29044473
Tray 50	–	29044474
Lid 10	–	29044475
Lid 20	–	29044476
Lid 50	–	29044477
Filter heater*	–	29044471
Bag sensor adaptor 2.5 m assembly†	Fiber cable for pH and DO control	28984189
Tub kit CBCU	1	29112187
Adjustable foot wrench‡	1	29112525

* One delivered with the rocker, additional needed for dual functionality.

† Depending on configuration, one or two fiber cables are delivered with the CBCU unit.

‡ One delivered with the rocker.

Related literature	Product code
UNICORN 7.0.2 Manual Package	29191514
OPC UaGateway Manual	29278101
UNICORN OPC Manual	29110887
UNICORN 7 software, data file	29135786
UNICORN 7 Academia Package	29203853
UNICORN 7 Process Development Package	29203854
UNICORN 7 Manufacturing Package	29203855
Disposable Cellbag bioreactors for WAVE Bioreactor systems, data file	28951136
Validation Support File UNICORN 7.0	28962650
ReadyToProcess WAVE 25, site preparation guide	29056702
ReadyToProcess WAVE 25, operating instructions	29009597
ReadyToProcess WAVE 25, system handbook	29009598

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GE Healthcare Europe, GmbH, Munzinger Strasse 5, D-79111 Freiburg, Germany
GE Healthcare Bio-Sciences Corp., 100 Results Way, Marlborough, MA 01752 USA
HyClone Laboratories, Inc., 925 W 1800 S, Logan, UT 84321 USA
GE Healthcare Japan Corporation, Sanken Bldg., 3-25-1, Hyakunincho, Shinjuku-ku, Tokyo 169-0073, Japan
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KA1658100118DF

GE Healthcare
Life Sciences

WAVE Bioreactor™ 200 system

WAVE Bioreactor 200 system (Fig 1) is part of GE Healthcare Life Sciences' ReadyToProcess platform of ready-to-use products. The system is a cell culture device for the production of recombinant proteins in mammalian and insect cell lines in batch, fed-batch, and perfusion culture. Culture medium and cells are loaded into a single-use, presterilized bag known as the Cellbag™ bioreactor. The Cellbag bioreactor is placed on an electric rocking base. The rocking motion of this base induces waves in the cell culture fluid within the Cellbag bioreactor to provide efficient mixing and gas transfer. The resulting environment within the Cellbag bioreactor can easily support 1×10^7 cells/mL. The Cellbag bioreactor requires no cleaning or sterilization, providing easy operation and protection against cross-contamination.

As part of ReadyToProcess platform, the WAVE Bioreactor brings flexibility and speed to upstream and downstream processing of biologicals. The product range comprises WAVE Bioreactor systems, WAVE Mixer™, tubing sealers and fusers, hollow fiber and normal flow filters, prepacked chromatography columns, and ÄKTA™ ready chromatography system with a disposable flow path, as well as the assemblies and connections in between. The platform is scalable from the lab bench to manufacturing.

WAVE Bioreactor 200 system delivers:

- Convenience: Presterilized, single-use Cellbag bioreactors protect against the risk of cross-contamination, require no cleaning, and involve minimal validation and they are supplied in a ready-to-use format
- Reliability: Cellbag bioreactors, including all fittings and filters, are supplied sterile and ready for use. They are suitable for cGMP commercial production and a biosafety cabinet is not required for inoculation or sampling
- Flexibility: Multiple instrument configurations for suspension, microcarrier, batch, fed-batch, or perfusion culture
- Versatility: The 200 system is capable of handling culture volumes from 10 to 100 L

Fig 1. The WAVE Bioreactor 200 system is suitable for culture volumes of 10 to 100 L.

System descriptions

The WAVE Bioreactor 200 system comprises integral rocking, temperature, weight, and airflow controllers. The self-contained system is designed for use with working culture volumes of 10 to 100 L in applications such as inoculum scale-up, R & D, commercial production, vaccine production, and antibody manufacture. For additional flexibility, optional modules including DO, CO_2, O_2, weight/perfusion, and pH control can be added while builtin Ethernet and MODBUS data ports allow communication with other software.

Applications

The WAVE Bioreactor system is suitable for use with anchorage-dependent cells in addition to cell suspensions and has applications in:

- Monoclonal antibodies
- Insect cell culture
- Virus production
- Growing pathogens or other high-containment systems
- Inoculum scale-up
- Protein expression
- Primary cell line expansion

Components

Touchscreen

The color touchscreen (Fig 2) located on the control panel of the WAVE Bioreactor 200 system enables the setup, control, and viewing of all cell culture parameters while data can be monitored graphically in real time. The main menu provides an overview of key operating conditions and it is the main access screen for all controls. Different control buttons are displayed depending on the options enabled. Pressing the desired button will take you to the respective control screen. The touchscreen is housed in a stainless steel enclosure and can be tilted and rotated for easier viewing.

Fig 2. The touchscreen provides easy access to all control functions.

Expansion slots

Optional modules such as the dissolved oxygen (DO), O_2, CO_2, pH, and dual system controllers can be added to standard WAVE Bioreactor systems to monitor and control additional parameters as your requirements change. These modules plug into the front and back instrument panels (Fig 3) of the base unit and are enabled via the instrument's configuration and calibration functions in order to display the module variables and controls on the color touchscreen. Spare racks are included for future instrument options.

Fig 3. Expansion slots are provided for the installation of optional instrumentation.

Linear electronic motor

An electric linear motor is used to rock the base units of the WAVE Bioreactor 200 system. Unlike geared motors, this electromagnetic device has only one moving part and provides greater reliability. The linear motor follows a preset and optimal speed and acceleration profile to provide the most effective wave for efficient low-shear mixing.

UNICORN™ DAQ

UNICORN DAQ 1.0 software facilitates real time data acquisition for the management and evaluation of results from cell cultures performed using up to four different WAVE Bioreactor systems connected to a single PC. The WAVE Bioreactor system can be connected directly or networked to the software providing a common platform and user interface for monitoring and storing result data. A dynamic graphical user interface informs you about the real-time status of the run being monitored. During a run, data is automatically saved to a local hard drive or server in a secure and unalterable result file for added security.

Quick-release bag holder

Rapid release Cam-lock levers secure the Cellbag bioreactor in place on the rocking platform allowing bags to be attached and removed in minutes. The holder design ensures that the Cellbag bioreactor is locked in the optimal position for oxygen transfer and mixing.

Stainless steel construction

The stainless steel housing of WAVE Bioreactor 200 system completely encloses the disposable Cellbag bioreactor and protects it from accidental damage. The housing is capable of containing potential spills. The WAVE Bioreactor 200 system is mounted on casters for mobility.

Optional components

pH monitor

The pH monitor provides amplification, display, and data transmission of pH allowing real-time measurement of pH in the Cellbag Bioreactor. The pH monitor was designed for use with pH sensor integrated into the WAVE Cellbag

Dissolved oxygen monitor

The DO monitor provides amplification, display, and data transmission of DO concentration allowing real-time measurement of DO concentration inside the Cellbag bioreactor. The DO monitor controller was designed for use with DO sensor integrated into the WAVE Cellbag, and it can increase the rocking rate or gas concentration automatically to maintain online control of DO.

O_2/air mix controller

The O_2/air mix controller connects to a supply of oxygen (and low pressure N_2 supply if required) to provide O_2/air concentrations between 0% and 50% O_2. The instrument controls enriched oxygen levels for insect cell/baculovirus and high culture density applications; it is also useful for maintaining low-oxygen environments for near-anaerobic applications.

CO_2/air mix controller

The CO_2/air mix controller connects to a supply of 100% CO_2 to provide CO_2/air concentrations between 0% and 15% CO_2. The instrument is useful for pH control of bicarbonate buffered cell culture media.

Temperature control

Temperature is regulated for single and dual WAVE Bioreactor systems (Fig 4).

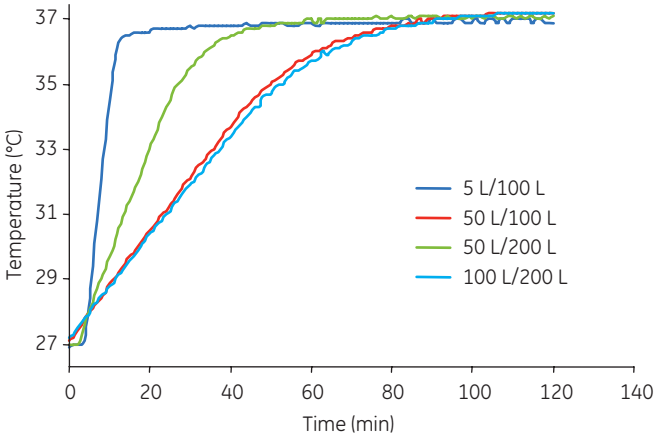

Fig 4. Temperature control from 27°C to 37°C in 5 L, 50 L in 100 L bag, 50 L, 100 L in 200 L bag.

Dual Cellbag control system

The WAVE Bioreactor 200 system can be configured for either single or dual Cellbag bioreactor control. In the dual-bag configuration, the menu on the touchscreen would display left- and right-bag values for certain parameters such as bag pressure and temperature. In the single-bag configuration, only data for the left-hand side bag is shown. Instruments configured as dual bag systems can be set to single-bag operation using the setup screen.

Analog output card

Up to eight channels of analog outputs are available as an option for controlling instrument variables such as rocking speed, weight, airflow, temperature, pH, DO, CO_2, and O_2 within their preset ranges. The DB25-pin analog output connector is located on the rear panel of the rocker base unit. Two analog output cards are required for dual-configured systems.

Loadcell

Electronic loadcell modules provide online measurement of Cellbag bioreactor weight and can be used for automated filling and harvesting of media. A built-in pump controller maintains a constant volume for perfusion operations. Loadcell modules are optional factory-installed accessories for WAVE Bioreactor 200 system.

Technical information and specifications

WAVE Bioreactor 200 system

Features	Touch panel operator interface
	Direct drive electronic linear motor
	Adjustable rocking rate from 4 to 25 rocks/min with acceleration control
	Adjustable rocking angle from 2° to 9° Integral temperature controller with heater Integral weight controller
	Integral airflow controller
	Integral PID controller for automatic temperature, O_2, CO_2, DO, and pH adjustment
	Real-time data monitoring
	RS-485 MODBUS communications port
	10Base-T Ethernet communications port Remote alarm contact and printer interface Stainless-steel containment enclosure
Dimensions (L × W × H)	Base unit: 1852 × 1096 × 1120 mm (73 × 43 × 44 in)
Weight (empty)	350 kg (780 lb)
Utilities	Voltage: 100-120/220-240 VAC
	Frequency: 50/60 Hz
	Maximum current: 15 A
	Power: 12 KVA
Environmental	This equipment is designed for use under the following conditions:
	• Indoor use
	• 5°C to 40°C
	• Up to 80% maximum relative humidity (rh) at 31°C decreasing linearly to 50% rh at 40°C

Ordering information

Product	Code number
SYSTEM200EH,CO2	28-4115-57
SYSTEM200EH,CO2,O2	28-4115-55
SYSTEM200EH, CO2,O2,AN	28-4115-52
SYSTEM200EH CO2 PHOPT AN	28-9849-54
SYSTEM200EH O2 DOOPT II AN	29-0042-81
SYSTEM200EH CO2 O2 DOOPT II PHOPT AN	29-0016-41
SYSTEM200EHD	28-9366-86
SYSTEM200EHD,CO2,AN	28-4115-45
SYSTEM200EHD,CO2,O2,AN	28-4115-44
SYSTEM200EHD CO2 PHOPT AN	28-9849-53
SYSTEM200EHD O2 DOOPT II AN	29-0042-82
SYSTEM200EHD CO2 O2 DOOPT II PHOPT AN	29-0016-37

Related literature

Disposable Cellbag bioreactors for the WAVE Bioreactor system, Data file	28-9511-36
ReadyToProcess connectivity, Data file	29-0138-84
WAVEPOD™ II Integrated Controller, Data file	28-9606-57
WAVE Bioreactor 2/10 and 20/50 systems, Data file	28-9520-58
WAVE Bioreactor 500/1000 system, Data file	29-0237-12

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GE Healthcare
Life Sciences

WAVE Bioreactor™ 500/1000 system

WAVE Bioreactor 500/1000 system (Fig 1) is part of GE Healthcare Life Sciences' ReadyToProcess platform of ready-to-use products. The system is a cell culture device for the production of recombinant proteins in mammalian and insect cell lines in batch, fed-batch, and perfusion culture. Culture medium and cells are loaded into a single-use, presterilized bag known as the Cellbag™ bioreactor. The Cellbag bioreactor is placed on an electric rocking base. The rocking motion of this base induces waves in the cell culture fluid within the Cellbag bioreactor to provide efficient mixing and gas transfer. The resulting environment within the Cellbag bioreactor can easily support 1×10^7 cells/mL. The Cellbag bioreactor requires no cleaning or sterilization, providing easy operation and protection against cross-contamination.

As part of ReadyToProcess platform, the WAVE Bioreactor brings flexibility and speed to upstream and downstream processing of biologicals. The product range comprises WAVE Bioreactor systems, WAVE Mixer™, tubing sealers and fusers, hollow fiber and normal flow filters, prepacked chromatography columns, and ÄKTA™ ready chromatography system with a disposable flow path, as well as the assemblies and connections in between. The platform is scalable from the lab bench to manufacturing.

WAVE Bioreactor 500/1000 system delivers:

- Convenience: Presterilized, single-use Cellbag bioreactors protect against the risk of cross-contamination, require no cleaning, and involve minimal validation and they are supplied in a ready-to-use format
- Reliability: Cellbag bioreactors, including all fittings and filters, are supplied sterile and ready for use. They are suitable for cGMP commercial production and a biosafety cabinet is not required for inoculation or sampling
- Flexibility: Multiple instrument configurations for suspension, microcarrier, batch, fed-batch, or perfusion culture
- Versatility: The 500/1000 system is capable of handling culture volumes from 50 to 500 L

Fig 1. The WAVE Bioreactor 500/1000 system is suitable for culture volumes of 50 to 500 L.

System descriptions

The WAVE Bioreactor 500/1000 system comprises integral rocking, temperature, weight, and airflow controllers. The self-contained system is designed for use with working culture volumes of between 50 and 500 L in applications such as inoculum scale-up, R & D, process development, commercial production, vaccine production, and antibody manufacture. For additional flexibility, optional modules including DO, CO_2, O_2, weight/perfusion, and pH control can be added while builtin Ethernet and MODBUS data ports allow communication with other software.

Applications

The WAVE Bioreactor system is suitable for use with anchorage-dependent cells in addition to cell suspensions and has applications in:

- Monoclonal antibodies
- Insect cell culture
- Virus production
- Growing pathogens or other high-containment systems
- Inoculum scale-up
- Protein expression
- Primary cell line expansion

Components

Touchscreen

The color touchscreen (Fig 2) located on the control panel of the WAVE Bioreactor 500/1000 system enables the setup, control, and viewing of all cell culture parameters while data can be monitored graphically in real time. The main menu provides an overview of key operating conditions and it is the main access screen for all controls. Different control buttons are displayed depending on the options enabled. Pressing the desired button will take you to the respective control screen. The touchscreen is housed in a stainless steel enclosure and can be tilted and rotated for easier viewing.

Fig 2. The touchscreen provides easy access to all control functions.

Expansion slots

Optional modules such as the dissolved oxygen (DO), O_2, CO_2, pH, and dual system controllers can be added to standard WAVE Bioreactor systems to monitor and control additional parameters as your requirements change. These modules plug into the front and back instrument panels (Fig 3) of the base unit and are enabled via the instrument's configuration and calibration functions in order to display the module variables and controls on the color touchscreen. Spare racks are included for future instrument options.

Fig 3. Expansion slots are provided for the installation of optional instrumentation.

Linear electronic motor

An electric linear motor is used to rock the base units of the WAVE Bioreactor 500/1000 system. Unlike geared motors, this electromagnetic device has only one moving part and provides greater reliability. The linear motor follows a preset and optimal speed and acceleration profile to provide the most effective wave for efficient low-shear mixing.

Quick-release bag holder

Rapid release Cam-lock levers secure the Cellbag bioreactor in place on the rocking platform allowing bags to be attached and removed in minutes. The holder design ensures that the Cellbag bioreactor is locked in the optimal position for oxygen transfer and mixing.

Optional components

pH Monitor

The monitor enables online measurement of pH using a single use electrochemical probe preinstalled in Cellbag bioreactors.

Dissolved oxygen monitor

The dissolved oxygen (DO) monitor provides amplification, display, and data transmission of DO concentration allowing real-time measurement of DO concentration inside the Cellbag bioreactor. The DO monitor controller was designed for use with miniature fiber optic dissolved oxygen probes (DOOPTPROBE), and it can increase the rocking rate automatically to maintain online control of DO.

O_2/air mix controller

The O_2/air mix controller connects to a supply of oxygen (and low pressure N_2 supply if required) to provide O_2/air concentrations between 0% and 50% O_2. The instrument controls enriched oxygen levels for insect cell/baculovirus and high culture density applications; it is also useful for maintaining low-oxygen environments for near-anaerobic applications.

CO_2/air mix controller

The CO_2/air mix controller connects to a supply of 100% CO_2 to provide CO_2/air concentrations between 0% and 15% CO_2. The instrument is useful for pH control of bicarbonate buffered cell culture media.

Analog output card

Up to eight channels of analog outputs are available as an option for controlling instrument variables such as rocking speed, weight, airflow, temperature, pH, DO, CO_2, and O_2 within their preset ranges. The DB25-pin analog output connector is located on the rear panel of the rocker base unit. Two analog output cards are required for dual-configured systems.

Loadcell

Electronic loadcell modules provide online measurement of Cellbag bioreactor weight and can be used for automated filling and harvesting of media. A built-in pump controller maintains a constant volume for perfusion operations. Loadcell modules are optional factory-installed accessories for WAVE Bioreactor 500/1000 system.

Technical information and specifications

WAVE Bioreactor 500/1000 system

Features	Touch panel operator interface
	Direct drive electronic linear motor
	Adjustable rocking rate from 4 to 25 rocks/min with acceleration control
	Adjustable rocking angle from 0.5° to 4° Integral temperature controller with heater Integral weight controller
	Integral airflow controller
	Integral PID controller for automatic temperature, O_2, CO_2, and pH adjustment
	Real-time data monitoring
	RS-485 MODBUS communications port
	10Base-T Ethernet communications port Remote alarm contact and printer interface Stainless-steel containment enclosure
Dimensions (L × W × H)	BASE unit: 201 × 124 × 160 cm (79 × 49 × 63 in)
	With KIT500EH: 226 × 124 × 160 cm (89 × 49 × 63 in)
	With KIT1000EH: 226 × 231 × 160 cm (89 × 91 in × 63 in)
Weight (empty)	BASE500/1000EH: 700 kg (1500 lbs)
	With KIT500EH: 925 kg (2000 lbs)
	With KIT1000EH: 1020 kg (2250 lbs)
Utilities	Voltage: 100-120/220-240 VAC
	Frequency: 50/60 Hz
	Maximum current: 15 A
	Power: 12 KVA
Environmental	This equipment is designed for use under the following conditions: • Indoor use • 5°C to 40°C • Up to 80% maximum relative humidity (rh) at 31°C decreasing linearly to 50% rh at 40°C

Ordering information

Product	Code number
SYSTEM1000EH CO2 O2 DOOPT PH AN	28-4115-59
SYSTEM1000EH DOOPT	28-4115-46
SYSTEM1000EH O2 DOOPT AN	28-4115-60
SYSTEM1000EH CO2 O2 DOOPT PH	28-4115-61
SYSTEM1000EH O2 DOOPT AN	28-4115-62
SYSTEM1000EH CO2 PH	28-4115-63
KIT500EH	28-4115-31
KIT1000EH	28-4115-32

Related literature

Disposable Cellbag bioreactors for the WAVE Bioreactor system, Data file	28-9511-36
ReadyToProcess connectivity, Data file	29-0138-84
WAVEPOD™ II Integrated Controller, Data file	28-9606-57
WAVE Bioreactor 2/10 and 20/50 systems, Data file	28-9520-58
WAVE Bioreactor 200 system, Data file	29-0237-13

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Japan

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Xcellerex™ XDR cell culture bioreactor systems

The Xcellerex XDR bioreactor product line offers the benefits of single-use technology and stirred-tank design in a modular, turnkey, bioreactor platform (Fig 1). Designed for scalability and robustness, the XDR bioreactor systems provide the performance and flexibility needed from process development to large-scale biopharmaceutical manufacturing. XDR bioreactor systems can be operated in batch, fed-batch, and perfusion modes.

XDR bioreactor systems offer the following benefits:

- Separation of gas and electrical power for enhanced safety
- Scalable and predictable stirred-tank performance up to 2000 L
- Single-use technology eliminates costly and time-consuming cleaning and cleaning validation
- Advanced automation and modular system design to support a variety of installation scenarios
- Process and operational support from staff with extensive manufacturing experience

System overview

The full line of XDR bioreactor systems are designed and characterized to deliver scalable process equivalence from 4.5 L to 2000 L working volume, in both GMP and non-GMP environments. The system design is based on the same foundational principles as conventional stainless steel bioreactors. Consistent vessel geometries, tight relationship between consumables and equipment features, and a host of accessories combine for an easily scalable, single-use product line. Traditional scaling methodology, based on measures such as shear, tip speed, power per unit volume, kLa, and specific process sensitivities, can be used during scale-up. Technology transfer using the XDR systems is straightforward, minimizing the need for costly and time-consuming process redesign. For enhanced utility across the bioreactor platform, the minimum working volume is as low as 20% of the maximum working volume.

Fig 1. Bioreactor system components: XDR vessel and X-Station mobile control console.

The bioreactor bag assembly (XDA) is disposed after culture termination and eliminates costly and time-consuming cleaning-in-place (CIP) and steam-in-place (SIP) operations. The XDA bag assembly is prepackaged with a low profile impeller, a variety of sparge components, filters, and tubing, for quick and hassle-free installation. The flexibility of single-use technology enables quick changeover between productions, for efficient equipment utilization. Interconnection of bioreactor bag and equipment is key in achieving the excellent performance that XDR bioreactor systems deliver.

The modularity of the XDR product line stems from three main subsystem components: bioreactor vessel with frame, I/O cabinet, and X-Station mobile control console. The XDR product line is further enhanced by the dual-panel I/O cabinet design, which separates gas management from electrical power. Additionally, high and low voltage power are in separate subsections of the main I/O cabinet. The system components can be used together for a complete turnkey system with true plug-and-play performance. Alternatively, the components can be used separately and integrated into existing infrastructure, for enhanced flexibility. The jacketed vessel has a consistent design and delivers integrated heating and cooling for efficient

temperature control throughout all scales. The versatile I/O cabinet houses all critical process instrumentation such as probe transmitters and peristaltic pumps: up to four internal and two external pumps are configurable. The gas management cabinet can be configured or customized with up to six mass flow controllers as well as up to four internal and two external pumps. The X-Station mobile control console is the heart of the product line's turnkey capability. The power and versatility of the X-Station allow for up to six XDR bioreactor systems to be controlled from one single control unit. This truly modular design creates a process-ready system upon delivery and also supports integration into a user-preferred automation platform.

XDR system components

Well-mixed bioreactor vessel

Constructed of 304 grade stainless steel (304 SS), the jacketed vessel enables efficient heat transfer and, together with an external temperature control unit (TCU), offers highly accurate temperature control of the cell culture. The bioreactor vessel features load cells for weight measurement and locking casters with leveling feet. Other features include a bioreactor bag tubing manager for convenient positioning and routing of the bag tubing and a high-performance, bottom-mounted, magnetically coupled drive system. Because of the bottom drive, there are no shafts to install from the top of the bioreactor vessel, minimizing ceiling height requirements. To aid in coupling and decoupling of the drive system with the bioreactor bag, motor lifting assistive devices are integral with the two largest bioreactor systems.

The systems are equipped with inlet and exhaust filter holders and vessel sidewall viewing ports. A lower sidewall port opening makes room for a sampling port as well as probes for pH, dissolved oxygen (DO), and temperature. An optional perfusion-specific bag loading door is available to accommodate cell retention devices. The 1000 L and 2000 L systems feature integrated bag loading doors that, along with the semiautomatic bag hoist, simplifies bag insertion without the need for climbing ladders. An efficient exhaust gas filter heater is also included to avoid condensate that could compromise exhaust filter performance.

The complete XDR bioreactor system product portfolio supports operating volumes from 4.5 L up to 2000 L. The smallest process development system is discussed in detail in a separate data file (29092927).

Versatile I/O cabinet

Two 304 SS I/O cabinets functionally separate devices for gas management, as well as pumps and transmitters for pH and DO measurement. Standard XDR gas and liquid management configurations cover the majority of cell culture applications. Probes on the bioreactor system provide real-time data, monitored throughout the process run using Wonderware™ software. Profibus™ communication standard is used for device communication and communication to the X-Station. For custom installations, direct Profibus communication between the I/O cabinet and other automation systems (e.g., Rockwell, DeltaV™, Honeywell, Siemens) can be accomplished.

Liquid management

The I/O cabinet can be configured with up to four pumps including on-off and variable speed peristaltic pumps. The on-off pumps utilize a Watson-Marlow™ 114 pump head, while the variable speed pumps utilize Watson-Marlow 313 or 520 pump heads depending on configuration. The pumps have ranges to support liquid addition or removal. They can also be programmed for fed-batch and perfusion culturing and easily calibrated using Wonderware software.

Gas management

Up to six mass flow controllers offer multiple sparging regimes, CO_2 abatement at large-scale, and overlay gas addition. The XDR systems include a gas manifold to distribute the various gases to the available bag destinations: sparger or headspace. The dual-panel XDR now includes a separate gas management cabinet.

Measurements of DO and pH

DO and pH can be measured using conventional polarographic sensors and glass electrodes, respectively. These sensors can be autoclaved prior to use in a specially designed probe sheath. Aseptic insertion into the bioreactor bag is conveniently done using single-use connector technology. Alternatively, an optical DO sensor and a single-use pH probe are available ready for use to minimize start-up time. The flexibility of the system allows the sensor technology to be mixed for use of conventional and single-use technologies simultaneously. All sensors are connected to the I/O cabinet transmitters. The dual-panel XDR includes options for Rosemount 56 and Mettler-Toledo MT-800 transmitters.

Measurement of dissolved carbon dioxide

Conventional, reusable, insertion-type probe technology is used for monitoring of dissolved carbon dioxide. A dedicated transmitter is available optionally for integration into the I/O cabinet.

Plug-and-play X-Station mobile control console

X-Station is a stand-alone, mobile control console featuring intuitive process control, data historian, and industrial-quality automation hardware and software (Fig 2). The control system provides real-time data acquisition, enables accurate process control, and offers convenient, real-time trending. X-Station is capable of measuring and controlling up to six XDR bioreactor systems simultaneously.

Inside the 304 SS cover is housed a scalable programmable logic controller (PLC)/programmable automation controller (PAC) and a server-class computer running user interface and data historian software. X-Station comes with a 19" touchscreen, industrial, wash down-resistant mouse, a QWERTY keyboard, and a built-in uninterruptible power supply (UPS). Profibus and Ethernet communication standards are included for equipment and local area network connectivity.

Fig 2. The X-Station mobile control console.

XDA bioprocessing consumables

The XDA bioreactor bag is an essential part of the process performance achieved with XDR bioreactor systems. Constructed with a contact layer of USP class VI-compliant low-density polyethylene (LDPE) plastic, the bioreactor bags are robust to withstand process conditions. All bioreactor bag assemblies incorporate a seal-less, bottom-mounted, impeller/sparger assembly with a centrally positioned integral magnet (Fig 3A). Installed in the bioreactor vessel, the impeller/sparger assembly couples with the magnetic drive head, creating a powerful and robust agitation system with minimal risk of seal leakage. Up to eight sparge elements are included in the impeller/sparge assembly (Fig 3B). Each sparge element can be configured with various porosities, drilled holes, or a combination of both to support both macro- and microsparging. Each of the standard sparge elements has been validated to provide out-of-the-box performance consistent with current cell culture practices.

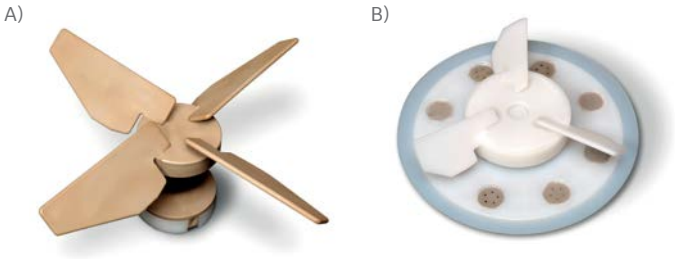


Fig 3. (A) Impeller for XDR-2000 with four pitched blades. (B) Impeller/sparger assembly for XDR-200 with three pitch blades and eight sparge elements.

The XDA bioreactor bags are available in Pro, Development, or Custom formats (Fig 4). Pro-type bags are available for all bioreactor systems and have validated sparge configurations, established based on customer feedback and our own biomanufacturing experience. Development bags are available for XDR-50 and XDR-200 bioreactor systems and differ from the Pro bags primarily in the configuration of the sparge elements. Development bags can be used in a broad array of process development activities where various micro- or macrosparging regimes are evaluated. Custom bioreactor bags can be modified with tubing type and quantity, connection type, filter element, or sparger configuration. Custom bags can also incorporate a CO_2-removal sparge wand to address processes sensitive to dissolved CO_2.

All bioreactor bags for cell culture include a magnetically coupled, M40e 40°, pitched-blade impeller with ceramic bearings. Ceramic bearings, originally developed for aggressive mixing applications and fermentation, provide excellent overall performance. The medical-grade ceramic bearings meet the relevant industry requirements for leachables, extractables, and particulates according to the bag validation guide (for more information, please contact your sales representative). Special impellers are available for microcarrier applications.

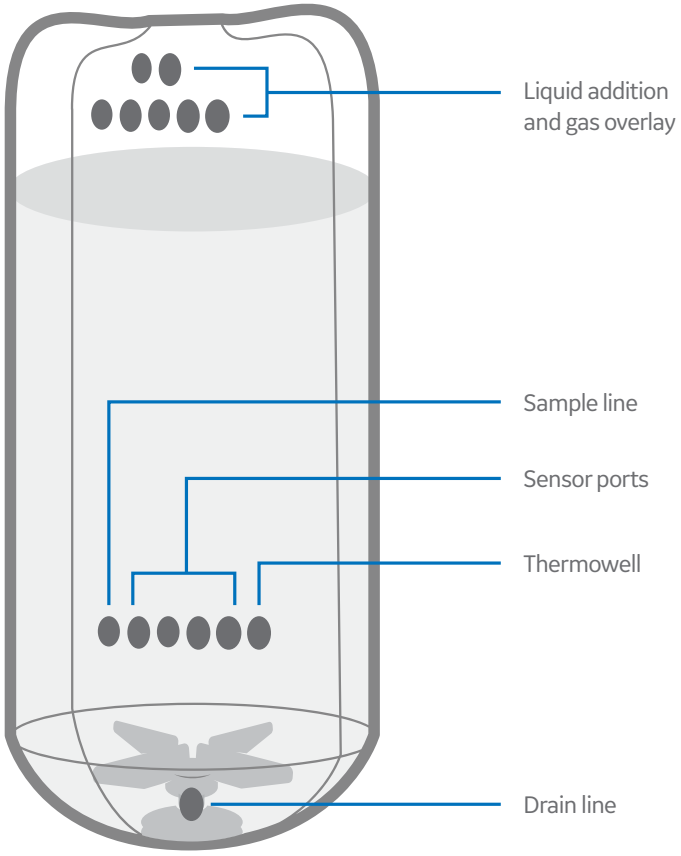


Fig 4. XDR-2000 Pro bag assembly.

Additional bag components include tubing with a combination of weldable sections and aseptic connectors for liquid addition/removal, a disposable pressure sensor, and filters for exhaust, sparge, and overlay/headspace gas. XDA bioreactor bags support both insertion-type reusable probes and single-use probes. Probe configurations include reusable probes only, single-use probes only, or mixed reusable and single-use probes. For details on probes, see section “Measurement of DO and pH”.

To assist in efficient bioreactor operation, a number of supplementary XDA bag-related accessories are optionally available. Like the main bioreactor bags, these accessories are tightly coupled to the equipment design to be adaptable to varied process requirements and to support operational efficiency. XDA accessories include seal-and-store sample manifolds, foam traps, X-Connect tubing sets, and exhaust filter tubing sets.

Qualification support

The XDR bioreactor systems are designed for use in environments that require 21 CFR Part 11 and GAMP™ 5. The systems are delivered with an operating manual, system specification, drawings to support qualification, and major component documentation. Industry standard installation and operation qualification (IQ/OQ) packages are available as an option.

Applications

XDR cell culture bioreactor systems have successfully been used to cultivate a wide range of cell types and organisms including CHO cells, Vero cells, and MDCK cells. In addition, a fermentor system is available for microbial applications including *E. coli*, *Pse domonas spp.*, and yeast (see data file 29092929). XDR bioreactor systems can be operated in batch, fed-batch, and perfusion (or chemostat) modes. Bioreactor bag design can be process-dependent, requiring customization for proper use and performance.

Customization

The XDR bioreactor offers standard configurations capable of addressing a broad set of cell culture applications. The product platform offers a variety of customizable options, which broaden its application. Contact your local GE representative to match your process to the XDR configuration that is right for your application.

Vessel specifications

Standard cell culture specifications are listed in Table 1.

Table 1. Specifications of standard configuration XDR cell culture bioreactor systems

	XDR-50*	XDR-200	XDR-500	XDR-1000	XDR-2000
Specifications					
Max. working volume (L)	50	200	500	1000	2000
Min. working volume (L)	22	40	100	200	400
Volume turn-down ratio	2.2:1	5:1	5:1	5:1	5:1
Aspect ratio (H/D)	2.25:1	1.5:1	1.5:1	1.5:1	1.5:1
Vessel	Jacketed 304 SS				
Filter heat assembly	1				
Additional lter heater assemblies (optional)	1				
Bag hoist	Not applicable	Not applicable	Not applicable	Semi-automatic	Semi-automatic
Impeller, M40e pitched-blade type	3 blades at 40° pitch	3 blades at 40° pitch	3 blades at 40° pitch	3 blades at 40° pitch	4 blades at 40° pitch
Custom bag assembly	3	3	4	4	4
Process instrumentation					
pH probes†	1 (2 optional)	2	2	2	2
DO probes†	1 (2 optional)	2	2	2	2
CO_2 probes (optional)	1 internal, 1 external				
MFC§ (standard)	4				
Additional MFC‡ (optional)	2				
Internal pumps (standard)	4 (2x low flow, 2x high flow)				
External pumps (optional)§	2				
Temperature control unit¶ (heating, kW/cooling, HP)	3/1	9/1.5	9/1.5	9/1.5	9/1.5
Load cells	3	4	4	4	4
X-Station control unit					
Interfaces	19”/52.4 mm touchscreen, wash-down compatible keyboard and mouse; includes built-in UPS				
Hardware	Rockwell™/Allen Bradley™				
Operator interface	Wonderware HMI††				
HMI†† Data Historian	Wonderware				
Compliance	21 CFR Part 11 compliant‡‡				

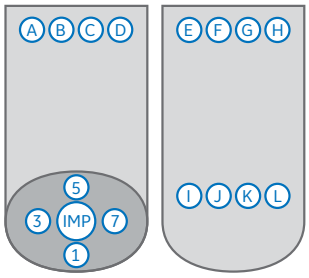
* For specifications of XDR-50 MO fermentation system, please see data file 29092929.
† Single-use or reusable probes
‡ Thermal mass flow controllers
§ External pumps are Profibus devices and might be Watson-Marlow 520, 620, or 720 series depending on required flow rate.
¶ Optional standalone heating/cooling TCU listed. Other TCU configurations available, including units that use facility chilled water/glycol.
†† Human-machine interface
‡‡ Customer will need to implement appropriate operating procedures to be fully 21 CFR Part 11 compliant. The XDR is built to support this two-part compliance.
Note: For specifications of XDR-10 bioreactor system, please see data file 29092927

Consumable specifications

Table 2. Specifications of standard configuration for XDA bags for XDR cell culture bioreactor systems

Product description	Product code

XDR-50 DEV



888-0356-C

Minimum volume: 22 L; nominal volume: 50 L; headspace volume: 13 L

Impeller: M40e, 3 blades, 8.5 in diameter, Di/Dt*: 0.61, 40° pitch, center

Film: ASI™ PL-01026/01077

A, B, D, G, H: 1 in of 1/4" × 3/8" C-Flex® 374

E: 1 in of 3/8" × 5/8" C-Flex 374

A, G, H (liquid additions): 3 in of 1/4 in × 7/16 in C-Flex 374 reduced to 48 in 1/8 in × 1/4 in C-Flex 374, plugged, pinch clamp

B, D (liquid additions): 48 in of 1/4 in × 7/16 in C-Flex 374, plugged, pinch clamp

C (vent filter): CFVTV0.2-33A filter (Meissner), T with 6 in of 1/2 in × 3/4 in C-Flex 374 terminated with ReadyMate™ connector, pinch clamp

E (liquid addition): 60 in of 3/8 in × 9/16 in Platinum-cured Silicon to 18 in of 3/8 in × 5/8 in C-Flex 374 terminated with ReadyMate connector, pinch clamp

F (headspace gas): pressure sensor, A50V002P2NV filter (Pall), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting, pinch clamp

I (RTD† thermowell): 1/4 in barb with dip tube for RTD† connection

J, K (probe ports): female Kleenpak™ port for probe connection

L (sample lines): 12 in of 1/8 in × 1/4 in C-Flex 374 terminated with female luer sampling port, pinch clamp (× 2)

M, O (liquid additions): 10 in of 3/4 in ×1 in C-Flex 374 terminated with ReadyMate connector

N (liquid addition): 18 in of 3/8 in × 5/8 in C-Flex 374 reduced to 18 in of 1/4 in × 7/16 in C-Flex 374, plugged, pinch clamp

Sparge 2: 2 m sintered disk

Sparge 4, 6: 2 m sintered disk with 5 × 0.5 mm drilled holes

Sparge 5: 20 m sintered disk

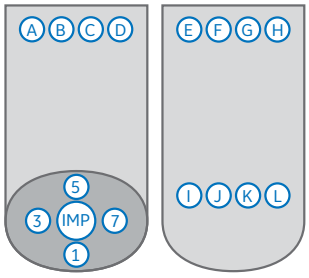
Sparge 8: 2 m sintered disk with 5 × 1 mm drilled holes

Sparge 2 and 5: tubing from each port combined to A50V002P2NV filter (Pall) to 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting, pinch clamp

Sparge 4, 6 and 8: tubing from each port combined to A50V002P2NV filter (Pall) to 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting, pinch clamp

Sparge 1 , 3 and 7 (drain): tubing from each port combined to 48 in of 3/8 in × 5/8 in C-Flex 374 terminated with ReadyMate connector, pinch clamp

XDR-50 PRO



888-0086-C

Minimum volume: 22 L; nominal volume: 50 L; headspace volume: 13 L

Impeller: M40e, 3 blades, 8.5 in diameter, Di/Dt*: 0.61, 40° pitch, center

Film: ASI PL-01026/01077

A, B, D, G, H: 1 in of 1/4 in × 3/8 in C-Flex 374

E: 1 in of 3/8 in × 5/8 in C-Flex 374

A, G, H (liquid additions): 3 in of 1/4 in × 7/16 in C-Flex 374 reduced to 48 in 1/8 in × 1/4 in C-Flex 374, plugged, pinch clamp

B, D (liquid additions): 48 in of 1/4 in × 7/16 in C-Flex 374, plugged, pinch clamp

C (vent filter): CFVTV0.2-33A filter (Meissner), T with 6 in of 1/2 in × 3/4 in C-Flex 374 terminated with ReadyMate connector, pinch clamp

E (liquid addition): 48 in of 3/8 in × 5/8 in C-Flex 374, plugged, pinch clamp

F (headspace gas): pressure sensor, A50V002P2NV filter (Pall), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting, pinch clamp

I (RTD† thermowell): 1/4 in barb with dip tube for RTD† connection

J, K (probe ports): female Kleenpak port for probe connection

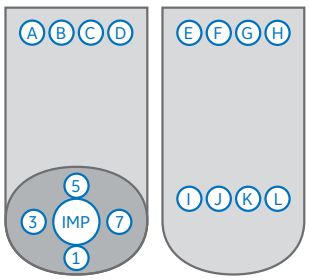
L (sample lines): 12 in of 1/8 in × 1/4 in C-Flex 374 terminated with female luer sampling port, pinch clamp (× 2)

Sparge 5: 2 m sintered disk, 48 in of 1/4 in × 7/16 in C-Flex 374 to A50V002P2NV filter (Pall) to 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting, pinch clamp

Sparge 1, 3 and 7 (drain): tubing from each port combined to 48 in of 3/8 in × 5/8 in C-Flex 374, plugged, pinch clamp

* Impeller diameter to bioreactor bag diameter
† Resistance temperature detectors

XDR-50 PRO FLEX



888-0086-F

Minimum volume: 22 L; nominal volume: 50 L; headspace volume: 13 L

Impeller: M40e, 3 blades, 8.5 in diameter, Di/Dt*: 0.61, 40° pitch, center

Film: ASI PL-01026/01077

A, B, D, G, H: 1 in of 1/4 in × 3/8 in C-Flex 374

E: 1 in of 3/8 in × 5/8 in C-Flex 374

A, G, H (liquid additions): 3 in of 1/4 in × 7/16 in C-Flex 374 reduced to 48 in 1/8 in × 1/4 in C-Flex 374, plugged, pinch clamp

B, D (liquid additions): 48 in of 1/4 in × 7/16 in C-Flex 374 terminated with ReadyMate connector, pinch clamp

C (vent filter): CFVTV0.2-33A1 filter (Meissner), T with 6 in of 1/2 in × 3/4 in C-Flex 374 terminated with ReadyMate connector, pinch clamp

E (liquid addition): 48 in of 3/8 in × 5/8 in C-Flex 374 terminated with ReadyMate connector, pinch clamp

F (headspace gas): pressure sensor, A50V002P2NV filter (Pall), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting, pinch clamp

I (RTD† thermowell): 1/4 in barb with dip tube for RTD† connection

J, K (probe ports): female Kleenpak port for probe connection

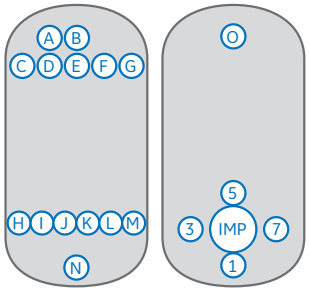
L (sample lines): 12 in of 1/8 in × 1/4 in C-Flex 374 terminated with female luer sampling port, pinch clamp (× 2)

Sparge 5: 2 m sintered disk, 48 in of 1/4 in × 7/16 in C-Flex 374 to A50V002P2NV filter (Pall) to 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting, pinch clamp

Sparge 6: 2 m sintered disk with 5 × 1 mm drilled holes, 48 in of 1/4 in × 7/16 in C-Flex 374 to A50V002P2NV filter to (Pall) 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting, pinch clamp

Sparge 1, 3 and 7 (drain): tubing from each port combined to 48 in of 3/8 in × 5/8 in C-Flex 374 terminated with ReadyMate connector, pinch clamp

XDR-200 DEV



888-0151-C

Minimum volume: 40 L; nominal volume: 200 L; headspace volume: 60 L

Impeller: M40e, 3 blades, 8.5 in diameter, Di/Dt*: 0.38, 40° pitch, 15° off center

Film: ASI PL-01026/01077

A, B (liquid additions): 3 in of 1/4 in × 7/16 in C-Flex 374 reduced to 120 in 1/8 in × 1/4 in C-Flex 374, plugged, pinch clamp

C, D, F (liquid additions): 18 in of 1/2 in × 3/4 in C-Flex 374 terminated with female Kleenpak connector, pinch clamp

E (headspace gas): pressure sensor, CFVTV0.2-33A filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting

G (liquid addition): 120 in of 1/2 in × 3/4 in C-Flex 374, plugged, pinch clamp

H (sample lines): 12 in of 1/8 in × 1/4 in C-Flex 374 terminated with female luer sampling port, pinch clamp (× 2)

I, J, K, L (probe ports): female Kleenpak port for probe connection

M (RTD† thermowell): 1/4 in barb with dip tube for RTD† connection

N (drain): 36 in of 1/2 in × 3/4 in C-Flex 374 terminated with female Kleenpak connector, pinch clamp

O (vent filter): KA3V002PV1G filter (Pall), T with 6 in of 1/2 in × 3/4 in C-Flex 374 terminated with female Kleenpak, pinch clamp

Sparge 1 and 5: 20 m sintered disk

Sparge 2, 6: 2 m sintered disk

Sparge 3 and 7: 2 m sintered disk with 5 × 1 mm drilled holes

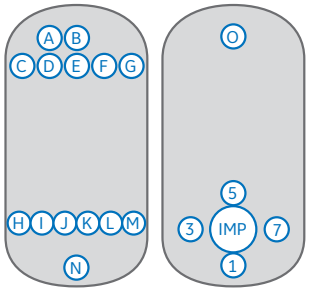
Sparge 4 and 8: 2 m sintered disk with 5 × 0.5 mm drilled holes

Sparge 1 & 5, 2 & 6, 3 & 7, 4 & 8: tubing from each port for each pair combined to 84 in of 1/8 in × 1/4 in C-Flex 374 to CFVTV0.2-33A filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting

* Impeller diameter to bioreactor bag diameter
† Resistance temperature detectors

XDR-200 PRO

888-0067-C



Minimum volume: 40 L; nominal volume: 200 L; headspace volume: 60 L

Impeller: M40e, 3 blades, 8.5 in diameter, Di/Dt*: 0.38, 40° pitch, 15° off center

Film: ASI PL-01026/01077

A, B (liquid additions): 3 in of 1/4 in × 7/16 in C-Flex 374 reduced to 120 in 1/8 in × 1/4 in C-Flex 374, plugged, pinch clamp

C, D, F (liquid additions): 18 in of 1/2 in × 3/4 in C-Flex 374 terminated with female Kleenpak connector, pinch clamp

E (headspace gas): pressure sensor, CFVTV0.2-33A filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting

G (liquid addition): 120 in of 1/2 in × 3/4 in C-Flex 374, plugged, pinch clamp

H (sample lines): 12 in of 1/8 in × 1/4 in C-Flex 374 terminated with female luer sampling port, pinch clamp (× 2)

I, J, K, L (probe ports): female Kleenpak port for probe connection

M (RTD† thermowell): 1/4 in barb with dip tube for RTD† connection

N (drain): 36 in of 1/2 in × 3/4 in C-Flex 374 terminated with female Kleenpak connector, pinch clamp

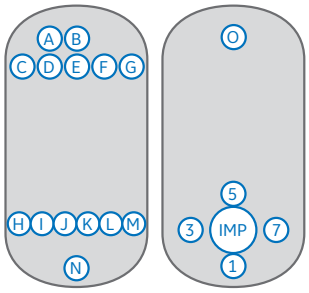
O (vent filter): KA3V002PV1G filter (Pall), T with 6 in of 1/2 in × 3/4 in C-Flex 374 terminated with female Kleenpak, pinch clamp

Sparge 1, 4 and 6: 2 m sintered disk

Sparge 1, 4 and 6: tubing from each port combined to 96 in of 1/8 in × 1/4 in C-Flex 374 to CFVTV0.2-33A filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting, pinch clamp

XDR-500 PRO

888-0070-C



Minimum volume: 100 L; nominal volume: 500 L; headspace volume: 125 L

Impeller: M40e, 3 blades, 10.5 in diameter, Di/Dt*: 0.35, 40° pitch, 15° off center

Film: ASI PL-01026/01077

A, B (liquid additions): 3 in of 1/4 in × 7/16 in C-Flex 374 reduced to 120 in 1/8 in × 1/4 in C-Flex 374, plugged, pinch clamp

C, D, F (liquid additions): 18 in of 1/2 in × 3/4 in C-Flex 374 terminated with female Kleenpak connector, pinch clamp

E (headspace gas): pressure sensor, CFVTV0.2-33A filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting

G (liquid addition): 120 in of 1/2 in × 3/4 in C-Flex 374, plugged, pinch clamp

H (sample lines): 12 in of 1/8 in × 1/4 in C-Flex 374 terminated with female luer sampling port, pinch clamp (× 2)

I, J, K, L (probe ports): female Kleenpak port for probe connection

M (RTD† thermowell): 1/4 in barb with dip tube for RTD† connection

N (drain): 36 in of 1/2 in × 3/4 in C-Flex 374 terminated with female Kleenpak connector, pinch clamp

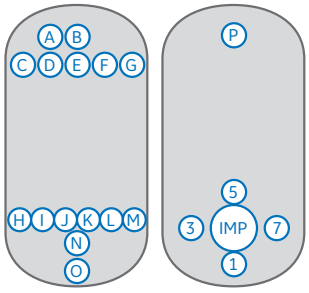
O (vent filter): KA3V002PV1G filter (Pall), T with 6 in of 1/2 in × 3/4 in C-Flex 374 terminated with female Kleenpak, pinch clamp

Sparge 1, 3, 5 and 7: 2 m sintered disk

Sparge 1, 3, 5 and 7: tubing from each port combined to 96 in of 1/4 in × 7/16 in C-Flex 374 to CFVTV0.2-33A filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting, pinch clamp

XDR-500 PRO FLEX

888-0070-F



Minimum volume: 100 L; nominal volume: 500 L; headspace volume: 125 L

Impeller: M40e, 3 blades, 10.5 in diameter, Di/Dt*: 0.35, 40° pitch, 15° off center

Film: ASI PL-01026/01077

A, B (liquid additions): 3 in of 1/4 in × 7/16 in C-Flex 374 reduced to 120 in 1/8 in × 1/4 in C-Flex 374, plugged, pinch clamp

C, D, F (liquid additions): 18 in of 1/2 in × 3/4 in C-Flex 374 terminated with ReadyMate connector, pinch clamp

E (headspace gas): pressure sensor, CFVTV0.2-33A1 filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting

G (liquid addition): 120 in of 1/2 in × 3/4 in C-Flex 374 terminated with ReadyMate connector, pinch clamp

H (sample lines): 12 in of 1/8 in × 1/4 in C-Flex 374 terminated with female luer sampling port, pinch clamp (× 2)

I, J, K, L (probe ports): female Kleenpak port for probe connection

M (RTD† thermowell): 1/4 in barb with dip tube for RTD† connection

N (sparge line): 96 in of 1/4 in × 7/16 in C-Flex 374 to CFVTV0.2-33A1 filter (Meissner), 3 in of 1/4 in × 7/16" C-Flex 374 terminated with instant tube fitting, pinch clamp with internal 2 mm drilled hole Sparge-T

O (drain): 36 in of 3/4 in × 1 in C-Flex 374 terminated with ReadyMate connector

P (vent filter): KA3V002PV1G filter (Pall), T with 6 in of 1/2 in × 3/4 in C-Flex 374 terminated with ReadyMate connector, pinch clamp

Sparge 1, 3, 5 and 7: 2 m sintered disk

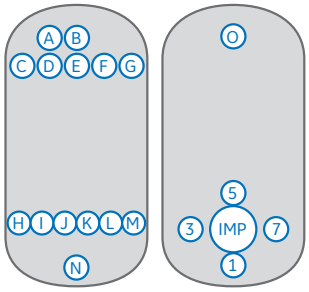
Sparge 1, 3, 5 and 7: tubing from each port combined to 96 in of 1/4 in × 7/16 in C-Flex 374 to CFVTV0.2-33A1 filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting, pinch clamp

* Impeller diameter to bioreactor bag diameter

† Resistance temperature detectors

XDR-1000 PRO

888-0071-C



Minimum volume: 200 L; nominal volume: 1000 L; headspace volume: 210 L

Impeller: M40e, 3 blades, 12.5 in diameter, Di/Dt*: 0.33, 40° pitch, 15° off center

Film: ASI PL-01026/01077

A, B (liquid additions): 3 in of 1/4 in × 7/16 in C-Flex 374 reduced to 120 in 1/8 in × 1/4 in C-Flex 374, plugged, pinch clamp

C, D, F (liquid additions): 18 in of 1/2 in × 3/4 in C-Flex 374 terminated with female Kleenpak connector, pinch clamp

E (headspace gas): pressure sensor, CFVTV0.2-33A filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting

G (liquid addition): 120 in of 1/2 in × 3/4 in C-Flex 374, plugged, pinch clamp

H (sample lines): 12 in of 1/8 in × 1/4 in C-Flex 374 terminated with female luer sampling port, pinch clamp (× 2)

I, J, K, L (probe ports): female Kleenpak port for probe connection

M (RTD† thermowell): 1/4 in barb with dip tube for RTD† connection

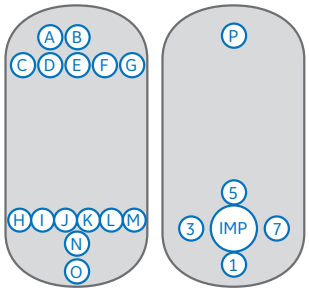
N (drain): 36 in of 1/2 in × 3/4 in C-Flex 374 terminated with female Kleenpak connector, pinch clamp

O (vent filter): KA3V002PV1G filter (Pall), T with 6 in of 1/2 in × 3/4 in C-Flex 374 terminated with female Kleenpak, pinch clamp

Sparge 1 to 8: 2 m sintered disk, all ports combined to 96 in of 1/4 in × 7/16 in C-Flex 374 to CFVTV0.2-33A filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting, pinch clamp

XDR-1000 PRO FLEX

888-0071-F



Minimum volume: 200 L; nominal volume: 1000 L; headspace volume: 210 L

Impeller: M40e, 3 blades, 12.5 in diameter, Di/Dt*: 0.33, 40° pitch, 15° off center

Film: ASI PL-01026/01077

A, B (liquid additions): 3 in of 1/4 in × 7/16 in C-Flex 374 reduced to 120 in 1/8 in × 1/4 in C-Flex 374, plugged, pinch clamp

C, D, F (liquid additions): 18 in of 1/2 in × 3/4 in C-Flex 374 terminated with ReadyMate connector, pinch clamp

E (headspace gas): pressure sensor, CFVTV0.2-33A filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting

G (liquid addition): 120 in of 1/2 in × 3/4 in C-Flex 374, ReadyMate Connector, pinch clamp

H (sample lines): 12 in of 1/8 in × 1/4" in C-Flex 374 terminated with female luer sampling port, pinch clamp (× 2)

I, J, K, L (probe ports): female Kleenpak port for probe connection

M (RTD† thermowell): 1/4 in barb with dip tube for RTD† connection

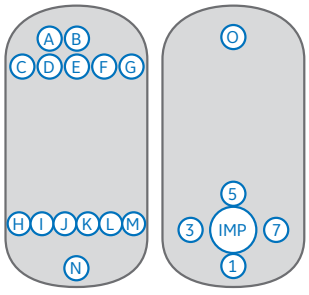
N (Sparge-T): 2 mm drilled hole Sparge-T

O (vent filter): 48 in of 1 in × 1 3/8 in C-Flex 374 terminated with ReadyMate connector

Sparge 1 to 8: 2 m sintered disk, all ports combined to 96 in of 1/4 in × 7/16 in C-Flex 374 to CFVTV0.2-33A filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting, pinch clamp

XDR-2000 PRO

888-0081-C



Minimum volume: 400 L; nominal volume: 2000 L; headspace volume: 500 L

Impeller: M40e, 4 blades, 16.5 in diameter, Di/Dt*: 0.34, 40° pitch, 15° off center

Film: ASI PL-01026/01077

A, B (liquid additions): 3 in of 1/4 in × 7/16 in C-Flex 374 reduced to 120 in 1/8 in × 1/4 in C-Flex 374, plugged, pinch clamp

C, D, F (liquid additions): 18 in of 1/2 in × 3/4 in C-Flex 374 terminated with female Kleenpak connector, pinch clamp

E (headspace gas): pressure sensor, CFVTV0.2-33A filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting

G (liquid addition): 120 in of 1/2 in × 3/4 in C-Flex 374, plugged, pinch clamp

H (sample lines): 12 in of 1/8 in × 1/4 in C-Flex 374 terminated with female luer sampling port, pinch clamp (× 2)

I, J, K, L (probe ports): female Kleenpak port for probe connection

M (RTD† thermowell): 1/4 in barb with dip tube for RTD† connection

N (drain): 36 in of 3/4 in × 1 in C-Flex 374 terminated with ReadyMate connector

O (vent filter): KA3V002PV1G filter (Pall), Y with 36 in of 3/4 in × 1 in C-Flex 374 terminated with ReadyMate connector

Sparge 1 to 8: 20 m sintered disk, all ports combined to 120 in of 1/2 in × 3/4 in C-Flex 374 to KA2V002PV1G filter (Pall), pinch clamp, 1-1/2" TC at filter inlet

* Impeller diameter to bioreactor bag diameter
† Resistance temperature detectors

XDR-2000 PRO FLEX

Minimum volume: 400 L; nominal volume: 2000 L; headspace volume: 500 L

Impeller: M40e, 4 blades, 16.5 in diameter, Di/Dt*: 0.34, 40° pitch, 15° off center

Film: ASI PL-01026/01077

A, B (liquid additions): 3 in of 1/4 in × 7/16 in C-Flex 374 reduced to 120 in 1/8 in × 1/4 in C-Flex 374, plugged, pinch clamp

C, D, F (liquid additions): 18 in of 1/2 in × 3/4 in C-Flex 374 terminated with ReadyMate connector, pinch clamp

E (headspace gas): pressure sensor, CFVTV0.2-33A filter (Meissner), 3 in of 1/4 in × 7/16 in C-Flex 374 terminated with instant tube fitting

G (liquid addition): 120 in of 1/2 in × 3/4 in C-Flex 374, ReadyMate conector, pinch clamp

H (sample lines): 12 in of 1/8 in × 1/4 in C-Flex 374 terminated with female luer sampling port, pinch clamp (× 2)

I, J, K, L (probe ports): female Kleenpak port for probe connection

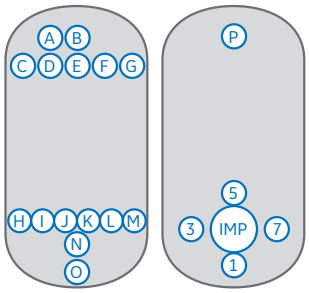
M (RTD† thermowell): 1/4 in barb with dip tube for RTD† connection

N (Sparge-T): 2 mm drilled hole Sparge-T

O (drain): 36 in of 1 in × 1 3/8" in C-Flex 374 terminated with ReadyMate connector

P (vent filter): KA3V002PV1G filter (Pall), Y with 36 in of ¾ in × 1" C-Flex 374 terminated with ReadyMate Connector

Sparge 1 to 8: 20 m sintered disk, all ports combined to 120 in of 1/2 in × 3/4 in C-Flex 374 to KA2V002PV1G filter (Pall), pinch clamp, 1-1/2" TC at filter inlet



888-0081-F

* Impeller diameter to bioreactor bag diameter
† Resistance temperature detectors

Opticap® XL and XLT Disposable Capsule Filters with Millipore Express® SHF 0.2 µm Hydrophilic Membrane

Opticap® XL and XLT capsule filters eliminate the time and expense associated with assembling, cleaning, and validating stainless steel housings.

Request More Information

Overview **Specifications** **Ordering Information** **Supporting Documentation** **Related Product & Applications**

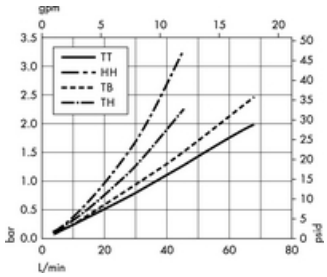
Specifications

Specifications (Autoclavable Capsules)

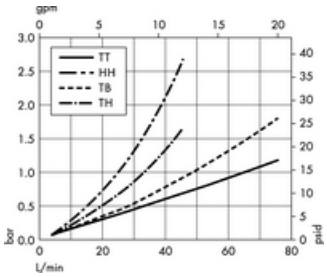
	Opticap XL3	Opticap XL5	Opticap XL10
Filtration Area	0.16 m²	0.29 m²	0.54 m²
Materials of Construction			
Filter	Polyethersulfone (PES)	Polyethersulfone (PES)	Polyethersulfone (PES)
Film Edge	Polypropylene	Polypropylene	Polypropylene
Supports	Polypropylene	Polypropylene	Polypropylene
Structural Components	Polypropylene/Polysulfone	Polypropylene/Polysulfone	Polypropylene/Polysulfone
Vent O-ring	Silicone (SI)	Silicone (SI)	Silicone (SI)
Vent/Drain	1/4 in. hose barb with double silicone O-ring seal		
Maximum Differential Pressure, bar (psid)	Forward: 6.9 bar (100 psid) intermittent @ 25 °C; 5.5 bar (80 psid) @ 25 °C; 1.0 bar (15 psid) @ 80 °C. Reverse: 2.1 bar (30 psid) @ 25 °C, intermittent		
Bubble Point	≥4000 mbar (58 psig) air with water		
Air Diffusion	≤9.1 mL/min @ 2.8 bar (40 psig) in water	≤16.4 mL/min @ 2.75 bar (40 psig) in water	≤30 mL/min @ 2.75 bar (40 psig) in water
Bacterial Retention	Quantitative retention of 10^7 CFU/cm^2 *Brevundimonas diminuta* (ATCC® 19146) per ASTM® F838-83 methodology		
Bacterial Endotoxins	Aqueous extraction contains ≤0.25 EU/mL as determined by the Limulus Amebocyte Lysate (LAL) Test		

Good Manufacturing Practices	These products are manufactured in a facility which adheres to FDA Good Manufacturing Practices.
Non-Fiber Releasing	Component materials meet the "non-fiber releasing" criteria as defined in 21 CFR 210.3 (b) (6).
Indirect Food Additive	All component materials meet the FDA Indirect Food Additive requirements cited in 21 CFR 177-182.

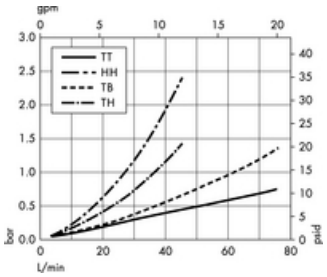
Typical Clean Water Flow Rate vs Pressure Drop (Autoclavable Capsules)



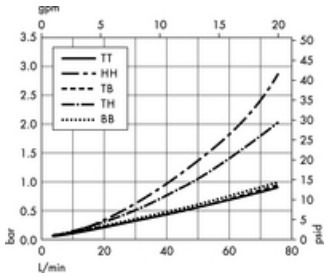
Opticap® XL 3 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane



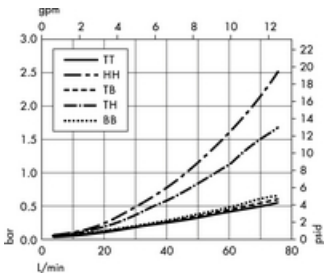
Opticap® XL 5 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane



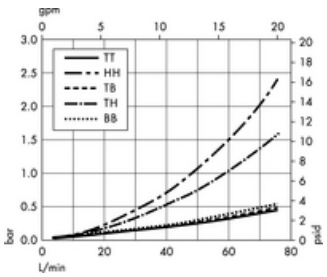
Opticap® XL 10 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane



Opticap® XLT 10 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane



Opticap® XLT 20 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane



Opticap® XLT 30 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane

Specifications (Sterile and Gamma Compatible Capsules)

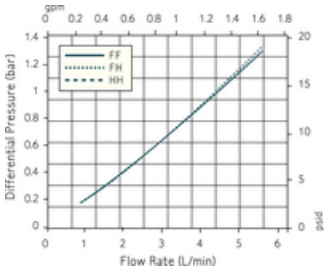
	Opticap XL 150	**Opticap XL 300**	**Opticap XL 600**
Filtration Area	220 cm²	480 cm²	970 cm²
Materials of Construction			
Filter	Polyethersulfone (PES)	Polyethersulfone (PES)	Polyethersulfone (PES)
Supports	Polyethylene	Polyethylene	Polyethylene
Structural Components	Gamma stable polypropylene/Polysulfone	Gamma stable polypropylene/Polysulfone	Gamma stable polypropylene/Polysulfone
Vent O-ring	Silicone (SI)	Silicone (SI)	Silicone (SI)
Vent/Drain	1/4 in. Hose Barb with double O-ring seal	1/4 in. Hose Barb with double O-ring seal	1/4 in. Hose Barb with double O-ring seal
Maximum Differential Pressure, bar (psid)	Forward: 6.9 bar (100 psid) intermittent @ 25 °C; 5.5 bar (80 psid) @ 25 °C; 1.0 bar (15 psid) @ 80 °C. Reverse: 2.1 bar (30 psid) @ 25 °C, intermittent		
Bubble Point	≥4000 mbar (58 psig) air with water		
Air Diffusion	≤1.4 mL/min @ 2.75 bar (40 psig) in water	≤2.8 mL/min @ 2.8 bar (40 psig) in water	≤5.8 mL/min @ 2.8 bar (40 psig) in water
Bacterial Retention	Quantitative retention of 10^7 CFU/cm^2 *Brevundimonas diminuta* (ATCC® 19146) per ASTM® F838-83 methodology		
Bacterial Endotoxins	Aqueous extraction contains ≤0.25 EU/mL as determined by the Limulus Amebocyte Lysate (LAL) Test		

TOC/Conductivity at 25 °C	Gamma sterilized filters meet the WFI requirements of USP <643> for Total Organic Carbon and USP <645> for Water Conductivity after a WFI flush of: 2 liter	Gamma sterilized filters meet the WFI requirements of USP <643> for Total Organic Carbon and USP <645> for Water Conductivity after a WFI flush of: 2.5 liters	Gamma sterilized filters meet the WFI requirements of USP <643> for Total Organic Carbon and USP <645> for Water Conductivity after a WFI water flush of: 3 liters
Oxidizable Substances	Will meet the USP Oxidizable Substances Test requirements after a water flush of ≥1 L	Will meet the USP Oxidizable Substances Test requirements after a water flush of ≥1 L	Will meet the USP Oxidizable Substances Test requirements after a water flush of ≥1 L
Sterilization			
Gamma compatible capsules	Gamma compatible to 45 kGy; 3 autoclave cycles of 60 min @ 123 °C; not in-line steam sterilizable		
Sterile capsules	3 autoclave cycles of 60 min @ 123 °C; not in-line steam sterilizable		
Sterility	Sterile capsules meet current USP and AAMI guidelines for sterility utilizing a validated sterilization cycle		
Component Material Toxicity	Component materials meet the criteria of the USP <88> Reactivity Test for Class VI Plastics. These products meet the requirements of the USP <88> Safety Test, utilizing a 0.9% sodium chloride extraction.		
USP Toxicity	Non-toxic per MEM elution ISO® 10993-5		
Good Manufacturing Practices	These products are manufactured in a facility which adheres to FDA Good Manufacturing Practices.		
Non-Particle Releasing	Passes USP test for particulates in injectables.		
Non-Fiber Releasing	Component materials meet the "non-fiber releasing" criteria as defined in 21 CFR 210.3 (b) (6).		
Indirect Food Additive	All component materials meet the FDA Indirect Food Additive requirements cited in 21 CFR 177-182.		

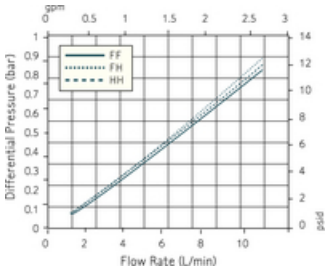
	Opticap XLT10	**Opticap XLT20**	**Opticap XLT30**
Filtration Area	0.57 m²	1.14 m²	1.71 m²
Materials of Construction			
Filter	Polyethersulfone (PES)	Polyethersulfone (PES)	Polyethersulfone (PES)
Film Edge	Polyethylene	Polyethylene	Polyethylene
Supports	Polyester	Polyester	Polyester
Structural Components	Gamma stable polypropylene/Polysulfone	Gamma stable polypropylene/Polysulfone	Gamma stable polypropylene/Polysulfone
Vent O-ring	Silicone (SI)	Silicone (SI)	Silicone (SI)
Vent/Drain	1/4 in. Hose Barb with double O-ring seal		
Maximum Differential Pressure, bar (psid)	Forward: 6.9 bar (100 psid) intermittent @ 25 °C; 5.5 bar (80 psid) @ 25 °C; 1.0 bar (15 psid) @ 80 °C. Reverse: 2.1 bar (30 psid) @ 25 °C, intermittent		
Bubble Point	≥4000 mbar (58 psig) air with water		
Air Diffusion	≤32.7 mL/min @ 2.75 bar (40 psig) in water	≤65.5 mL/min @ 2.75 bar (40 psig) in water	≤98.2 mL/min @ 2.75 bar (40 psig) in water
Bacterial Retention	Quantitative retention of 10^7 CFU/cm^2 *Brevundimonas diminuta* (ATCC® 19146) per ASTM® F838-83 methodology		
Bacterial Endotoxins	Aqueous extraction contains ≤0.25 EU/mL as determined by the Limulus Amebocyte Lysate (LAL) Test		

TOC/Conductivity	Autoclaved filter meets the WFI requirements of USP <643> for Total Organic Carbon and USP <645> for Water Conductivity after a WFI water flush of: 11 liters at 25 °C	Autoclaved filter meets the WFI requirements of USP <643> for Total Organic Carbon and USP <645> for Water Conductivity after a WFI water flush of: 22 liters at 25 °C	Autoclaved filter meets the WFI requirements of USP <643> for Total Organic Carbon and USP <645> for Water Conductivity after a WFI water flush of: 33 liters at 25 °C
Oxidizable Substances	Will meet the USP Oxidizable Substances Test requirements after a water flush of ≥1.5 L	Will meet the USP Oxidizable Substances Test requirements after a water flush of ≥3 L	Will meet the USP Oxidizable Substances Test requirements after a water flush of ≥4.5 L
Sterilization			
Gamma compatible capsules	Gamma compatible to 45 kGy; 3 autoclave cycles of 60 min @ 123 °C; not in-line steam sterilizable		
Sterile capsules	3 autoclave cycles of 60 min @ 123 °C; not in-line steam sterilizable		
Sterility	Sterile		
Component Material Toxicity	Component materials meet the criteria of the USP <88> Reactivity Test for Class VI Plastics. These products meet the requirements of the USP <88> Safety Test, utilizing a 0.9% sodium chloride extraction.		
USP Toxicity	Non-toxic per MEM elution ISO® 10993-5		
Good Manufacturing Practices	These products are manufactured in a facility which adheres to FDA Good Manufacturing Practices.		
Non-Fiber Releasing	Component materials meet the "non-fiber releasing" criteria as defined in 21 CFR 210.3 (b) (6).		
Indirect Food Additive	All component materials meet the FDA Indirect Food Additive requirements cited in 21 CFR 177-182.		

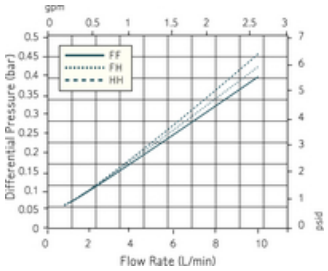
Typical Clean Water Flow Rate vs Pressure Drop (Sterile and Gamma Compatible Capsules)



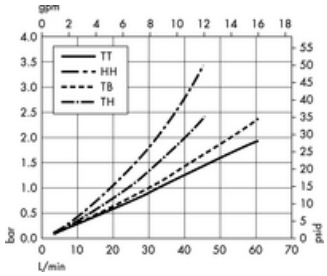
Opticap® XL 150 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane



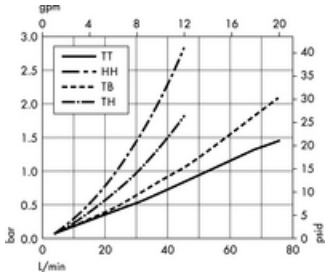
Opticap® XL 300 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane



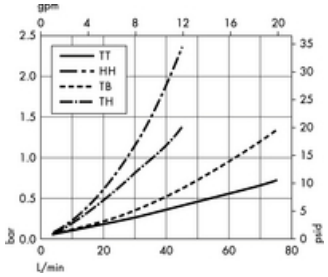
Opticap® XL 600 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane



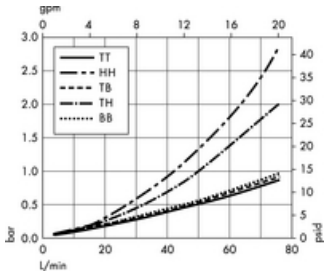
Opticap® XL 3 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane



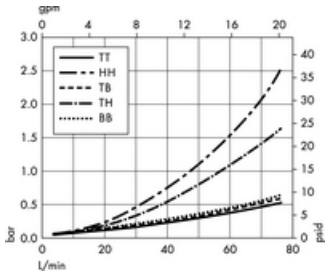
Opticap® XL 5 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane



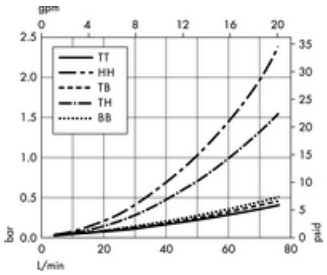
Opticap® XL 10 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane



Opticap® XLT 10 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane



Opticap® XLT 20 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane



Opticap® XLT 30 Capsule Filters with 0.2 µm Millipore Express® SHF Membrane

Recently Viewed

Opticap® XL and XLT Disposable Capsule Filters with Millipore Express® SHF 0.2 µm Hydrophilic Membrane
Opticap® XL and XLT capsule filters eliminate the time and expense associated with assembling, cleaning, and validating stainless steel housings.

Recommended Products

Opticap® Gamma Compatible XL 3 Millipore Express® SHC...

Opticap® XL4 Durapore® 0.22 µm 9/16 in. HB/HB

Opticap® XL5 Durapore® 0.22 µm 1-1/2 in. TC/TC

MASTERFLEX®

TUBING APPLICATION GUIDE

PUSHING THE BOUNDARIES OF PERISTALTIC PUMP TECHNOLOGY WITH UNIQUE FORMULATIONS

Cole-Parmer®
Delivering Solutions You Trust

MasterFlex® Tubing Application Guide

Pharmaceuticals • Drug Discovery

BioPharm Plus Tubing

Longer life (up to five times) and lower spallation compared to other platinum silicone tubing. Ultra-smooth inner surface. Biocompatible for sensitive applications. Autoclavable. Meets FDA, USP Class VI, and EP standards, and exceeds 3A sanitary standards. Max temp: 450°F (232°C).

Applications: filtration; fermentation; dispensing solutions and media.

- Excellent pumping accuracy for high repeatability and consistent performance over time
- Smooth inner bore results in less particle entrapment
- Low spallation maintains purity of fluid
- No leachable additives or plasticizers to impart taste or contamination
- Sterilize to maintain system sterility
- Tolerates high-pressure applications

Biopharmaceuticals • Nutraceuticals

C-FLEX® Tubing

Excellent biocompatibility; contains no toxic materials. Heat sealable and weldable. Autoclavable. Meets FDA and USP Class VI standards. Max temp: 275° F (135°C).

Applications: biopharmaceutical processing and storage; botanical production.

- Combines the biocompatibility of silicone with chemical resistance of Tygon®, but with longer pumping life
- Nonpyrogenic, noncytotoxic, and nonhemolytic properties maintain purity and sterility of fluids
- Low protein binding ensures minimal degradation or loss of sample
- Chemically resistant to acids and bases for longer tubing life

Pharmaceutical • Life Science • Electronics • Semiconductor

PharmaPure® Tubing

Nontoxic and nonhemolytic, excellent biocompatibility. Longest pumping life of any high-performance formulation; low extractability. Autoclavable. Meets FDA, EP, and USP Class VI standards. Max temp: 275°F (135°C).

Applications: sterile filling; filtration; transfer of cell media.

- Ultra-low spallation maintains fluid purity and extends the life of filters
- Low permeability provides barrier to chemicals that damage tubing
- Tolerates continuous-pressure applications up to 40 psi (2.7 bar)
- Long tubing life means time and cost savings

Chemical • Printing • Automotive

Chem-Durance™ Tubing

Best combination of pumping life and chemical resistance. Excellent durability. Plasticizer-free inner liner provides low spallation. Autoclavable. Meets FDA standards. Max temp: 165°F (74°C).

Applications: transfer of sensitive fluids; ink and solvent production.

- Chemical-resistant inner liner allows use with harsh chemicals
- Low spallation maintains purity of fluid
- Flexible outer jacket dissipates heat generated from rollers for longer tubing life
- Hydrophobic, smooth-bore inner liner means negligible absorption of fluids or leachables

Chemical • Pharmaceutical • Food & Beverage

Tygon® Chemical Tubing

Best chemical resistance of any Tygon formulation. Compatible with many popular solvents. Autoclavable. Complies with FDA 21 CFR 177.2600 criteria. Max temp: 135°F (57°C).

Applications: disinfectant transfer; dispensing of food additives.

- Plasticizer- and oil-free to ensure accurate results from analytical tests; does not yield taste into fluids
- Clear tubing for easy flow monitoring
- Sterilize to maintain system sterility
- Low gas permeability and extractability maintains integrity of fluid
- Very good chemical compatibility affords longer tubing life

Chemical • Manufacturing • Semiconductor

Viton® Tubing

Resistant to corrosives, solvents, and oils at elevated temperatures. Low gas permeability. Max temp: 400°F (205°C).

Applications: transfer harsh chemicals through process line.

- Exclusive Masterflex® formulation—highest fluorine content of any Viton for enhanced chemical compatibility
- Tolerates some of the harshest chemicals used in the semiconductor industry
- Resistant to corrosive solvents and aliphatic and aromatic hydrocarbons
- Ultra-low gas permeability maintains integrity of fluid

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Fax: 847-247-2929
www.coleparmer.com

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www.coleparmer.ca

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Fax: 91-22-6716-2211
www.coleparmer.in

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FREE TECHNICAL APPLICATIONS ASSISTANCE!

Electronics • Semiconductor • Industrial • Chemical • Food & Beverage

PTFE Tubing

The only peristaltic-compatible PTFE tubing available!

Excellent fluid purity, chemical resistance, and very low gas permeability. Autoclavable. Meets FDA and USP Class VI standards. Max temp: 500°F (260°C).

Applications: vulcanization; feeding and metering of aggressive chemicals; dispensing of fruit extracts and flavoring.

- Chemically inert; offering the best chemical resistance of any pump tubing
- Rigid tubing structure provides tolerance for high-pressure applications up to 100 psi (6.8 bar)
- Inert fluoropolymer will not leach into or absorb out of fluid being pumped

Pharmaceutical • Water • Wastewater

High-Pressure PharMed® BPT and High-Pressure Norprene® Tubing

High-Pressure PharMed BPT: Over 10,000 hours of tubing life. Heat sealable, bondable, and autoclavable. Resists ozone and UV radiation. Meets FDA and USP Class VI standards. NSF-listed. Max temp: 270°F (135°C).
High-Pressure Norprene: Up to 10,000 hours tubing life. Resists heat, ozone, acids, and alkalis. Heat sealable, non-aging, non-oxidizing, and autoclavable. Best choice for pressure/vacuum applications. Max temp: 270°F (135°C).

Applications: sterile filtration; chemical injection.

- Thick-walled tubing withstands pressures up to 100 psi (6.8 bar) with precise, repeatable flow
- Noncytotoxic and nonhemolytic properties make PharMed BPT ideal for tissue and cell culture work
- Chemical-resistant Norprene handles a variety of chemicals and solutions

GLOSSARY

Cytotoxic—having a toxic effect on cells
Hemolytic—causing the destruction of red blood cells
Leachables—chemicals released from tubing that may contaminate fluid being pumped
Pyrogenic—showing measurable traces of bacterial endotoxins
Spallation—the generation of particles from the inner bore of the tubing

MASTERFLEX® RESOURCES ONLINE

Pump system selection:
Masterflex.com/pumpconfigurator

Tubing compatibility:
Masterflex.com/mflexChem

Peristaltic pump applications:
Masterflex.com/pumpSolutions

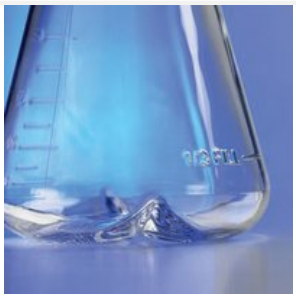
SIGMA-ALDRICH

CLS431407 SIGMA

Corning® Erlenmeyer baffled cell culture flasks

250 mL Erlenmeyer Flask w/ Vent Cap, polycarbonate, sterile, 50/cs

Synonym: **Corning Erlenmeyer flasks, baffled cell culture flasks, cell culture flasks, conical flasks, plastic Erlenmeyer flasks, shaker flasks**



SDS SIMILAR PRODUCTS

eCl@ss 32040501

Properties

Related Categories	Corning, Corning Erlenmeyer Flasks and Fernbach Flasks, Polycarbonate, Corning Flasks, Corning LSE Equipment, Corning LSE Shakers & Vortexers, More...
material	**polycarbonate flask**
	polypropylene cap (Easy-Grip vent)
	wide-mouth
sterility	**sterile; γ-irradiated**
feature	**disposable**
	graduations 25 mL
	graduations
packaging	**pack of 1**
	case of 50
mfr. no.	**Corning, 431407**
flask capacity	**250 mL**
neck diam.	**25 mL**
suitability	**suitable for (ideal for all shaker culture applications as well as liquid handling and storage)**

Show Fewer Properties

Description

General description

Corning® Erlenmeyer Baffled Cell Culture Flasks

Corning baffled bottom Erlenmeyer flasks are sterile, disposable and are ideal for all shaker culture applications as well as liquid handling and storage. Like all Corning flasks, the flasks are certified nonpyrogenic and sterile. The 125 mL through 1 L Erlenmeyer flasks are available with standard two-position plug seal caps or filtered vent caps. The 2 L and 3 L flasks are available with vent caps.

Features and Benefits:

More Robust
- Polycarbonate construction: USP Class VI material provides excellent optical clarity and mechanical strength
- Unlike PETG, flasks will not collapse when autoclaving media or sanitizing waste
- Unlike glass, flasks will not break when dropped

More Reliable
- RNase- and DNase-free
- Molded-in-graduations for accuracy
- Vent cap option for continuous gas exchange while ensuring sterility and preventing leakage
- Individual packaged and radiation sterilized
- All flasks have the highest Sterility Assurance Level (SAL) of 10-6
- Certified nonpyrogenic
- Made from optically clear polycarbonate
- Ideal for shaker culture applications
- Vent caps available for applications requiring sterile gas exchange
- Sterilized by gamma radiation and certified nonpyrogenic

Note: Erlenmeyer flasks can be used with Corning LSE™ orbital shaker

Legal Information

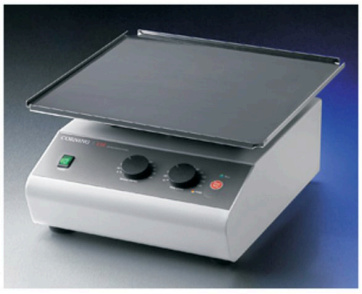
Corning is a registered trademark of Corning, Inc.

LSE is a trademark of Corning, Inc.

Price and Availability

SKU-Pack Size	Availability	Price (USD)	Quantity
CLS431407-50EA		**641.70**	

TOP



Corning™ LSE™ Low Speed Orbital Shaker GSA/VA

Ideal for staining and destaining fragile gels, washing blots and general mixing applications

Manufacturer: Corning™ 6780FP

Catalog No. 10-320-813

$1,363.68 / Case

Description

- Gentle motion prevents foaming of liquids
- Analog control with easy-turn knobs
- 19mm orbit for blotting, gel staining and general mixing
- Speed can be set from 3 to 60rpm
- Timer can be set for up to 2 hours or for continuous operation
- Safe for cold room and incubator use
- 120V, 50/60Hz

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Specifications

Model	6780-FP	Speed Range	3 to 60rpm
Orbit	1.9cm	Hertz	50/60Hz
Length (English) Exterior	10 in.	Length (Metric) Exterior	25.5cm
Plug Type	US	Voltage	120V
Height (English)	6 in.	Height (Metric)	16cm
Type	Orbital shaker	Width (English)	12.5 in.

Width (Metric)	32cm
Electrical Requirements	120V 50/60Hz

Controller Type	Analog

Thermo Scientific Forma Series 3
Water Jacketed CO_2 Incubator

SPECIFICATIONS AND ORDERING INFORMATION

Specifications

Temperature	
Control	±0.1°C
Range	5°C above ambient to 55°C (131°F)*
Uniformity	±0.2°C @ 37°C (98.6°F)**
Tracking Alarm	+/-1°C
Temperature Safety	
Sensor	Precision thermistor
Controller	Independent analog electronic
Setability	0.1°C
CO_2/O_2	
CO_2/O_2 Control	Better than ±0.1%
CO_2 Range	0–20%
O_2 Range	1–20%
Inlet Pressure	15 PSIG (1.0 bar)
CO_2 Sensor	T/C or IR
O_2 Sensor	Fuel cell
Readability & Setability	0.1%
Tracking Alarm	+/-1%
Humidity	
RH	Ambient to 95% @ 37°C (98.6°F)
Humidity Pan	3.2 qt. (3.0 liters) standard
Display (opt.)	In 1% increments
Fittings	
Fill Port	3/8" hose (barbed)
Drain Port	1/4" hose (barbed)
Access Port	1.3" (3.3cm) with removable silicone plug with filter
CO_2 Inlet	1/4" hose (barbed)
Unit Heat Load	
115V/230V	344 BTUH (100 Watt)
Shelves	
Dimensions	18.5" x 18.5" (47.0cm x 47.0cm)
Construction	Stainless steel, perforated
Surface Area	2.4 sq. ft. (0.2 sq. m)
Max. per Chamber	40.8 sq. ft. (3.8 sq. m)
Standard, Maximum	4, 17

Construction	
Water Jacket Volume	11.7 gal. (43.5 liters)
Interior Volume	6.5 cu. ft. (184.1 liters)
Interior	Type 304, mirror finish, stainless steel
Exterior	18 gauge, cold-rolled steel, powder coated
Outer Door Gasket	Four-sided, molded, magnetic vinyl
Inner Door Gasket	Removable, cleanable, feather-edged, silicone
Electrical	
4110/4120/4130/4140	115V, 50/60 Hz, 3.6 FLA (operating range 90–125V)
4111/4121/4131/4141	230V, 50/60 Hz, 2.0 FLA (operating range 180–250V)
Circuit Breaker/ Power Switch	6 Amps/2 Pole
Convenience Receptacle	75 Watts max. (one per chamber)
Plug	115V: NEMA 5-15P Plug 230V: CEE 7/7 Plug
Alarm Contacts	Power interruption; deviation of temp, CO_2, O_2, RH; customer connections through jack on back of unit
Data Outputs (opt.)	USB (standard), 4–20 milliamp (optional)
Dimensions	
Exterior	26.0"W x 39.5"H x 25.0 USB Port (standard), 4-20 ma (optional)"F-B (66.0cm x 100.3cm x 63.5cm)
Interior	21.3"W x 26.8"H x 20.0"F-B (54.1cm x 68.1cm x 50.8cm)
Weight	
Net	265 lb (120.2 kg)
Net Operational	365 lb (165.6 kg)
Shipping (Motor)	324 lb (147.0 kg)

Orderimg Information

Cat. No.	CO_2	O_2	Voltage
4110	T/C	No	115
4111	T/C	No	230
4120	IR	No	115
4121	IR	No	230
4130	T/C	Yes	115
4131	T/C	Yes	230
4140	IR	Yes	115
4141	IR	Yes	230

All units are UL Listed to United States and Canadian requirements and bear the CE Mark.
*50°C (122°F) on Model 4120 (4121), 45°C (113°F) on Models 4130 (4131) and 4140 (4141).
**Truncated

See how Thermo Scientific CO_2 incubators provide optimal cell growth.
Learn more at www.thermoscientific.com/co2incubators

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BRCO2FORMA3 0115

Thermo SCIENTIFIC
Part of Thermo Fisher Scientific

General Specifications

	LOCATOR 4	LOCATOR 4 PLUS	LOCATOR 6 PLUS	LOCATOR 8	LOCATOR 8 PLUS	LOC ATOR JR.	LOCATOR JR. PLUS
HEIGHT (Including lid)[1]	37.5" (95.25 cm)	40" (101.6 cm)	38" (96.5 cm)	37.5" (95.25 cm)	40" (101.6 cm)	27.5" (69.85 cm)	30" (76.2 cm)
DIAMETER	22" (55.8 cm)	22" (55.8 cm)	26" (55.8 cm)	22" (55.8 cm)	22" (55.8 cm)	22" (55.8 cm)	22" (55.8 cm)
VESSEL VOLUME	110L	111L	165L	110L	111L	50L	51L
LN2 CAPACITY, LIQUID PHASE STORAGE	90L	91L	134L	90L	91	40	41L
VAPOR PHASE LN_2 CAPACITY	25L	26L	39L	25L	26L	20L	21L
STATIC LN_2 EVAPORATION RATE - L/DAY	.65	.80	.80	.40	.58	.65	.80
LIQUID PHASE CAPACITY (Ampules actually submerged in liquid nitrogen.)	2916 ampules* or 3600 ampules**	3240 ampules* or 4000 ampules**	4860 ampules or 6000 ampules**	1800 ampules	2000 ampules	1296 ampules* or 1600 ampules**	1620 ampules* or 2000 ampules**
VAPOR PHASE CAPACITY (Ampules are kept slightly above the level of liquid mitrogen.)	2268 ampules* or 2800 ampules**	2592 ampules* or 3200 ampules**	3888 ampules* or 4800 ampules**	1400 ampules	1600 ampules	972 ampules* or 1200 ampules**	1296 ampules* or 1600 ampules**

1 The liquid nitrogen level monitor will add 1 inch to these heights. The transportation cart will add 4 inches to these heights.

* Using Nalgene cryoboxes with a 9 x 9 ampule configuration.

** Using Nalgene System 100™ cryoboxes with a 10 x 10 ampule configuration. (Nalgene System 100™ ampules or equivalent are needed.)

Environmental Conditions

Operating: 17°C - 27°C; 20% to 80% relative humidity, non-condensing. Installation Category II (over-voltage) in accordance with IEC 664. Pollution Degree 2 in accordance with IEC 664. Altitude limit: 2,000 meters.

Storage: -25°C to 65°C; 10% to 85% relative humidity.

Thomas Scientific

Thermo Scientific Nalgene

Cryogenic Storage Boxes for Locator™ and Locator Plus Systems

Email This Page Print Page

DESCRIPTION

Request A Customer Account

Obtain a comprehensive solution when plastic is preferred to fiberboard. Thermo Scientific™ Nalgene™ Cryogenic Storage Boxes for Locator™ and Locator Plus Systems fit in Thermo Scientific stainless-steel, ultra-low temperature freezer racks.

Please Enter Your Order Info

Filter by: Avail. Qty ▼ CLEAR FILTERS

PRODUCT DETAIL

5149D15

Mfr. No. CS509X3

Description

Ampule Box, 25-Place For Locator 8

List Price/Quantity	Total
$723.86 /CS (**80**/CS) 0	$0.00

5149D25

List Price/Quantity	Total

Mfr. No. CS509X4

Description

Ampule Box, 81-Place For Locator 4

List Price/Quantity	Total
$556.87 /CS (**40**/CS) 0	$0.00

5149D35

Mfr. No. CS509X5

Description

Ampule Box, 81-Place For Locator Jr

List Price/Quantity	Total
$276.88 /CS (**20**/CS) 0	$0.00

1187N35

Mfr. No. CS509X10

Description

4" Vial Box for 5mL Nalgene Vials, 81 vials/box

List Price/Quantity	Total
$40.85 /EA (**1**/EA) 0	$0.00

1187N36

Mfr. No. CS509X24

Description

2" Vial Box for 1 & 1.5mL Nalgene Vials, 100 vials/box

List Price/Quantity	Total
$159.70 /CS (**10**/CS) 0	$0.00

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You must be logged in to add items to a list. Please log in here.

$0.00 (0 Items)

ADD TO SHOPPING CART

Write A Review

Rating (required)

Comments (required)

QUATTROFLOW™ Fluid Systems
Part of Pump Solutions Group
A DOVER COMPANY

Spec Sheet QF150S
Effective: **October 2014**
Replaces: **NEW**

QF150S

Quaternary Diaphragm Pumps
Multiple-Use – Biotech/Biopharma

Features

- 4-piston technology
- Includes control panel
- Gentle product treatment
- No particle generation
- Low pulsation
- Linear flow characteristic
- Hygienic design
- Self-priming
- Safe dry-run operation
- Also available as single-use version

Applications

- Filtration systems (TFF, etc.)
- Chromatography systems
- Feeding pump
- Virus filtration
- Sterile filtration

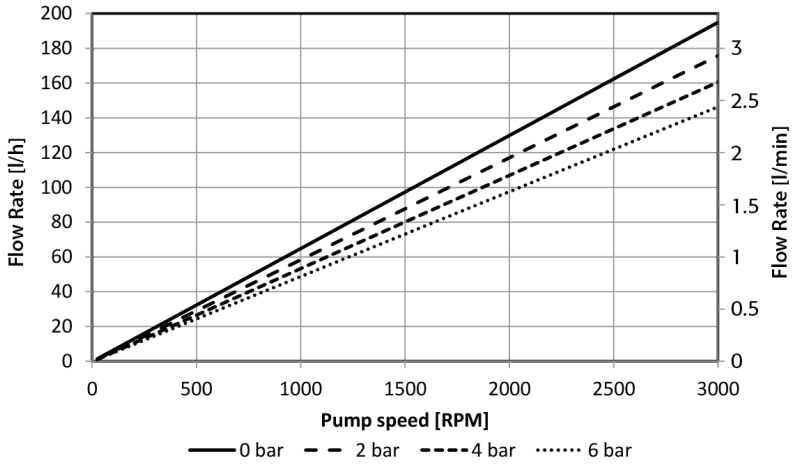
Technical Data

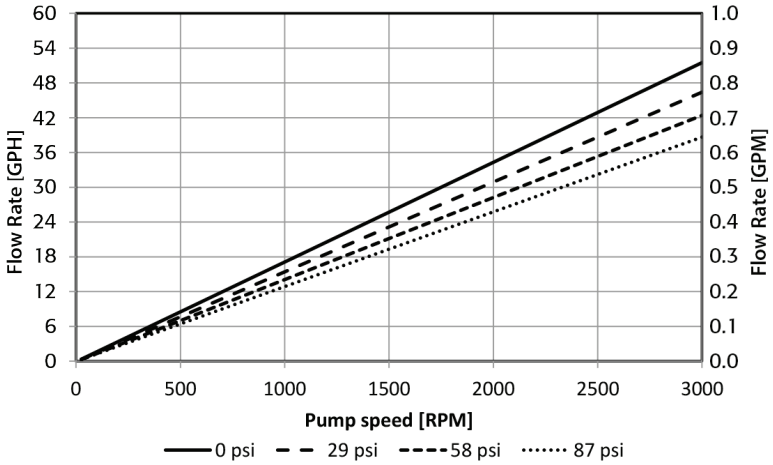
	QF150S Standard Motor
Flow Rate Maximum:	
Eccentric Shaft 5°	180 l/h (48 gph)
Flow Rate Minimum:	
Eccentric Shaft 5°	1 l/h (0.26 gph)
Pressure:	
Temperature of Fluid < 40° C (104° F)	6 bar (87 psi)
Temperature of Fluid > 40° C (104° F)	4 bar (58 psi)
Maximum Temperature:	
Fluid	80° C (176° F)
CIP	90° C (194° F)
SIP	130° C (260° F)
Autoclave	130° C (260° F)
Suction Lift Dry at 3000 rpm:	
Eccentric Shaft 5°	2 - 3 m (6.6 - 9.8 ft)
Volume Specifications:	
Approximated Volume per Revolution at Free Output	1.2 ml
Filling Volume Without Connectors	15 ml
Connection Specification (Standard):	
Connectors	1/4" TC
Position of Connectors	Inline
Number of Flow Directions	4

	QF150S Standard Motor
Product Wetted Materials (Standard):	
Pump Housing	SS316L
Valve Plate	SS316L
Diaphragms	TPE
Valves	EPDM
O-rings	EPDM
Certificates/Proofs (Optional):	
Elastomere (product wetted)	USP <88> Cl. VI; FDA21CFR177; BSE/TSE Safe
Stainless Steel Parts (product wetted)	3.1; Surface Roughness; Ferrite Content
Motor (Standard):	
Rated speed	3000 min-1 (50 Hz)
Voltage	230/115 V
Power	0.05 KW
Pump Dimension with Motor and Housing:	
Length	280.5 mm (11.04")
Width	115 mm (4.53")
Height	184 mm (7.24")
Pump Weight with Motor and Housing:	
	8.4 kg (19 lb.)

Other connection specifications, materials and motors available on request.

Performance Charts





Accessories

Power Box

- Plug & Play installation
- Protects system and pump from overpressure
- Configurable pressure switch setpoint
- Reset button for pump reset
- To be used with pressure switch (also available)

QUATTROFLOW™ Fluid Systems
Part of Pump Solutions Group
A DOVER COMPANY

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PSG PUMP SOLUTIONS GROUP
A DOVER COMPANY

QUATTROFLOW™ Fluid Systems
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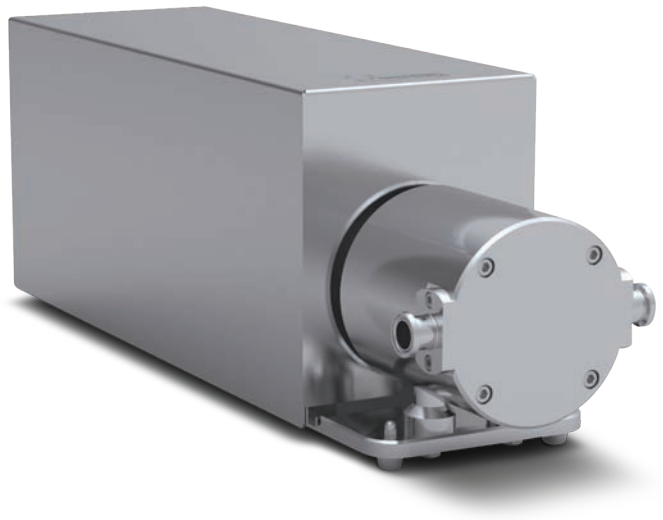
Spec Sheet QF1200S
Effective: **October 2014**
Replaces: **NEW**

QF1200S

Quaternary Diaphragm Pumps
Multiple-Use – Biotech/Biopharma



Features

- 4-piston technology
- Gentle product treatment
- No particle generation
- Low pulsation
- Linear flow characteristic
- Hygienic design
- Self-priming
- Safe dry-run operation
- Also available as single-use version

Applications

- Filtration systems (TFF, etc.)
- Chromatography systems
- Feeding pump
- Virus filtration
- Sterile filtration

Technical Data

	QF1200S Standard Motor
Flow Rate Maximum:	
Eccentric Shaft 3°	800 l/h (211 gph)
Eccentric Shaft 5°	1,200 l/h (317 gph)
Flow Rate Minimum*:	
Eccentric Shaft 3°	10 l/h (2.64 gph)
Eccentric Shaft 5°	20 l/h (5.3 gph)
Pressure:	
Temperature of Fluid < 40° C (104° F)	6 bar (87 psi)
Temperature of Fluid > 40° C (104° F)	4 bar (58 psi)
Maximum Temperature:	
Fluid	80° C (176° F)
CIP	90° C (194° F)
SIP	130° C (260° F)
Autoclave	130° C (260° F)
Pump Speed Range:	
rpm	30 - 2,400
Suction Lift Dry at 1800 rpm:	
Eccentric Shaft 3°	2.5 - 3 m (8.2-9.8 ft)
Eccentric Shaft 5°	4 - 4.5 m (13.1-14.7 ft)
Volume Specifications:	
Approximated Volume per Revolution at Free Output	9.6 ml (5°) 5.8 ml (3°)
Filling Volume Without Connectors	75 ml

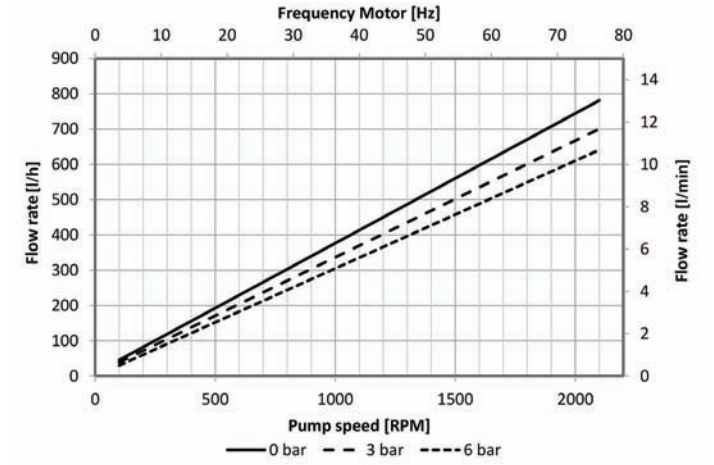
	QF1200S Standard Motor
Connection Specification (Standard):	
Connectors	3/4" TC
Position of Connectors	Inline
Number of Flow Directions	4
Product Wetted Materials (Standard):	
Pump Housing	SS316L
Valve Plate	SS316L
Diaphragms	TPE
Valves	EPDM
O-rings	EPDM
Certificates/Proofs (Optional):	
Elastomere (product wetted)	USP <88> Cl. VI; FDA21CFR177; BSE/TSE Safe
Stainless Steel Parts (product wetted)	3.1; Surface Roughness; Ferrite Content
Motor (Standard):	
Rated speed	1375 min-1 (50 Hz)
Voltage	230/400 V
Power	0.37 KW
Pump Dimension with Motor and Housing:	
Length	487 mm (19.17")
Width	159 mm (6.26")
Height	210 mm (8.27")
Pump Weight with Motor and Housing:	
	24 kg (53 lb.)

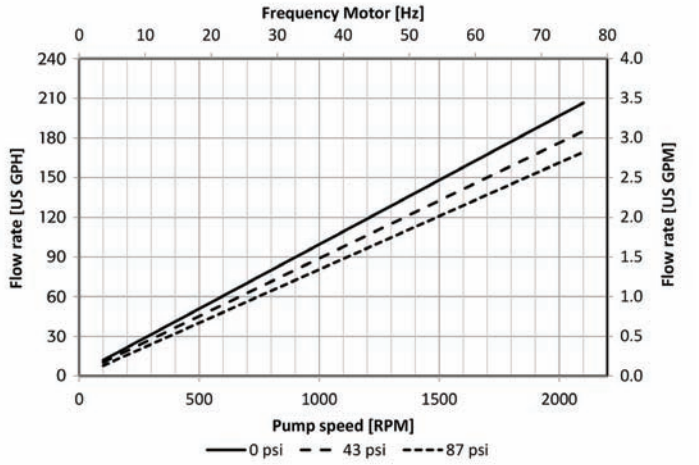
Other connection specifications, materials and motors available on request.

* When using pump with control box: 20 l/h (5.28 gph) and 40 l/h (10.6 gph)

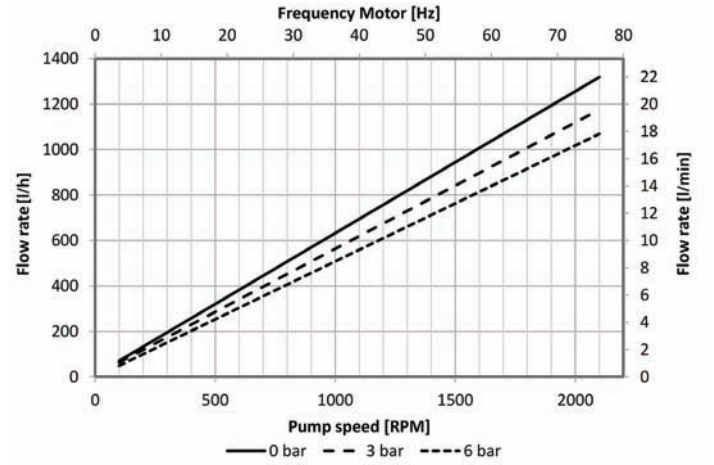
Performance Charts

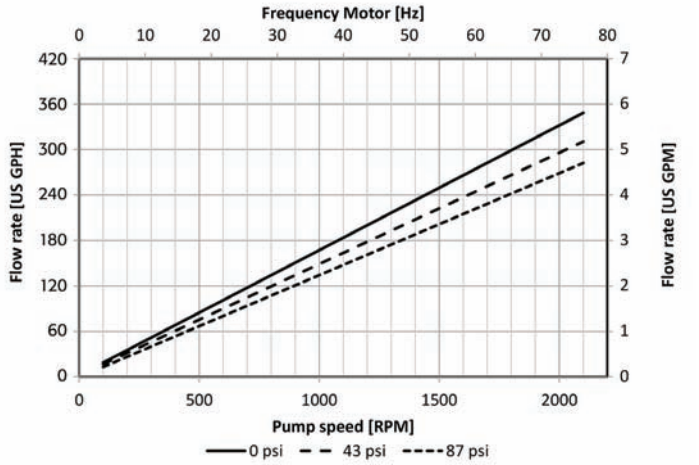
Eccentric Shaft: 3°





Eccentric Shaft: 5°





Depending on the selected motor/frequency drive combination, the motor frequency and the resulting pump speed might differ.

Accessories

Control Box

- Variable speed controller with integrated touch pad for manual speed control
- Configurable for remote speed control with 4-20 mA analogue input
- 230V / 50 Hz or 115 V / 60 Hz
- Hygienic 1.4301 housing, IP 54
- Easy plug & play installation

Power Box

- Plug & Play installation
- Protects system and pump from overpressure
- Configurable pressure switch setpoint
- Reset button for pump reset
- To be used with pressure switch (also available)

Diaphragm Sensor

- Sensor installed in ring drive unit
- Detection of all liquids
- Signal output to a controller, if diaphragm is ruptured

QUATTROFLOW™ Fluid Systems
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A DOVER COMPANY

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www.quattroflow.com
info@almatec.de

825 series hygienic pump

800 series

Watson-Marlow Bredel

FEATURES

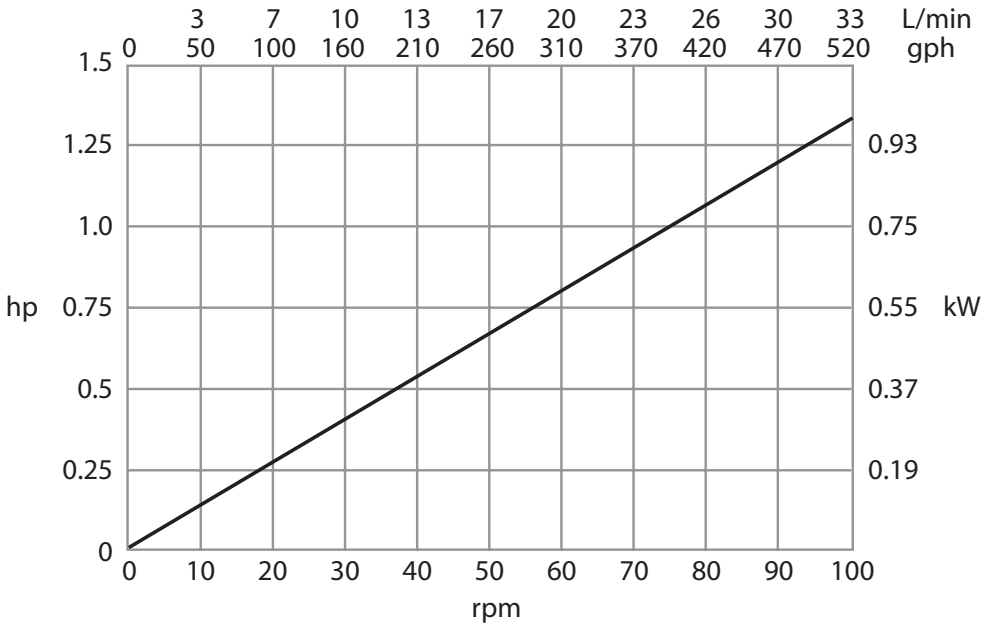
- Flow rates up to 575 gph (36 L/min) at 50 psi (3.5 bar) continuous pressure
- Clean-in-place and steam-in-place sterilization at full velocity with no bypass required
- Ideal for viscous or shear sensitive products
- Bioprene or STA-PURE tube certified to USP Class VI and FDA approved with hygienic stainless steel connectors
- Bioprene tubing available in two hardnesses for pressures up to 30 psi (2 bar) and 50 psi (3.5 bar). STA-PURE tubing is rated for pressures up to 50 psi (3.5 bar)
- Pumpheads to accept B5 output flange-mounted gear motors in a range of single and three phase fixed and electronic variable speeds
- Hinged door with only two captive bolts makes tube inspection and change extremely simple and safe
- Explosion proof version available
- Options include stainless steel pushbar and swivel caster set for mobile applications and a wide variety of connectors

2 warranty

24 hour duty

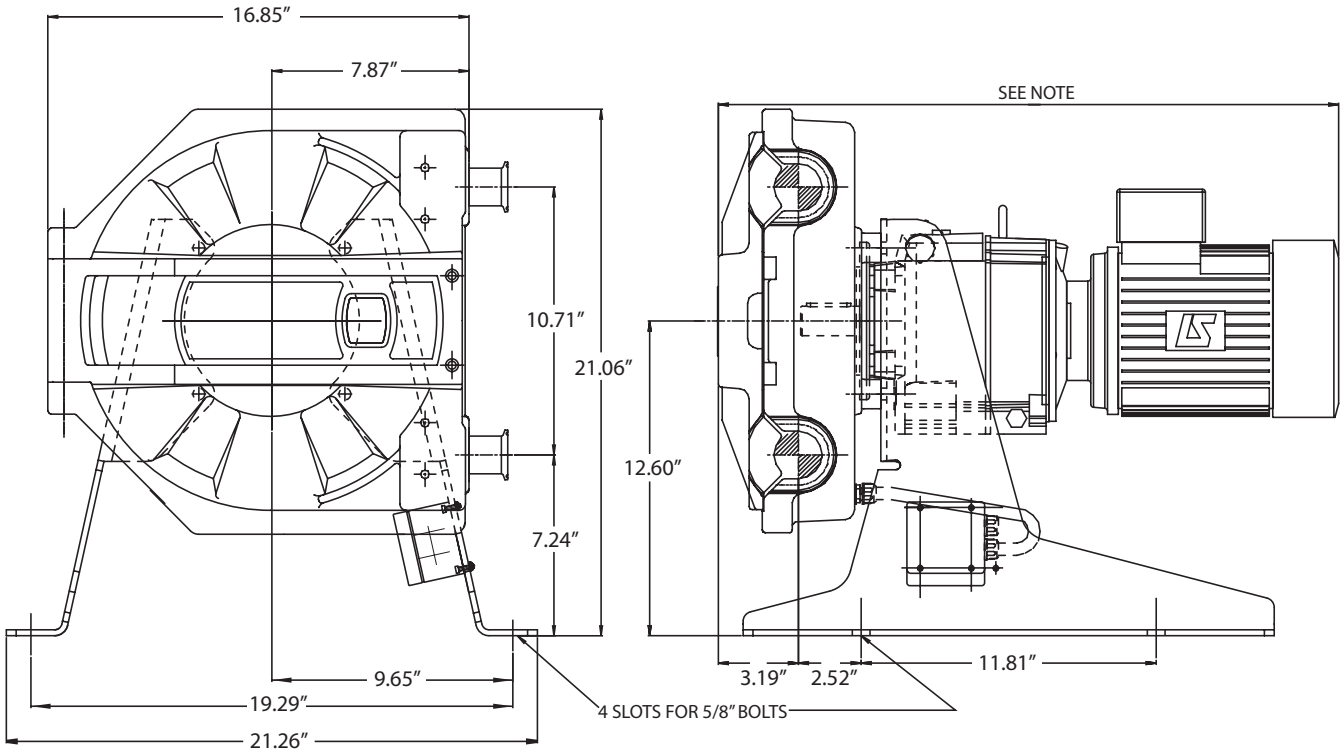
PERFORMANCE

Speed (rpm)	Flow rate (gph)	Flow rate (L/min)	Fitted Motor Power (hp)
30	157	10	0.75
56	293	18	1.0
84	439	28	1.5
101	528	33	2.0



For variable speed units and other gearing or build options, please contact your local representative, or the Watson-Marlow Bredel Applications Engineering department.

DRAWINGS



Length dependant on selection of gearbox and motor

SPECIFICATIONS

Environment Temperature	40°F to 104°F
Fluid Temperature	-32°F to 175°F
Max Operating Speed	109 rpm
Max Pressure	50 psi continuous (3.5 Bar)
Suction Pressure	Up to 28 ft water
Pump weight	Dependant upon drive. Nominally 250 lbs
Control ratio	Dependant upon VFD selection
Noise	< 75dB(A) at 1m
Supply	230/460/575 3ph 60Hz, 115/230 1ph 60Hz
Door Switch	50 Watt, 240VAC (not suitable for XP environments)
Power	Up to 2 hp

MATERIALS OF CONSTRUCTION

Component	Material
Pumphead body	Aluminum alloy with epoxy polyester powder coat finish
Pumphead door	Aluminum alloy with epoxy polyester powder coat finish
Pumphead rotor hub	Aluminum alloy with epoxy polyester powder coat finish
Rotor rollers	Stainless steel 316
Support frame	Stainless steel 304
Door fixings	Stainless steel 304
Motor fixings	Zinc plated high tensile steel bolts, stainless steel nuts and washers
Frame fixings	Stainless steel 304

ORDER INFORMATION

Element and Connector product codes

Description	Sanitary	Description	Partcode
Bioprene TM hose	088.0250.E0M	1" Tri-clamp, 316SS	089.0250.00T
Bioprene TH hose	088.0250.E0H	1" Tri-clamp, PVDF	089.0250.00K
Sta-pure hose	089.0250.000	1" Male Cam & Groove, 316SS	089.0250.00Q

All flow rates shown were obtained pumping water at 68°F with zero suction and delivery heads.

Watson-Marlow Bredel Pumps
37 Upton Technology Park
Wilmington, MA 01887
Tel: 800 282 8823 Fax: 978 658 0041
www.watson-marlow.com support@watson-marlow.com

MILLIPORE

- *Ideal for particle and microorganism removal*
- *Excellent resistance to thermal and hydraulic stress*
- *Validated to withstand multiple sterilization cycles*
- *Scalable — from bench-top to full-scale production*
- *Wide selection of configurations to meet your process needs*

DATA SHEET

Sterilizing-grade Durapore® 0.22 µm Hydrophobic Filters

Reliable filters for the sterile filtration of gases and liquids

Durapore hydrophobic membrane cartridges and capsules are sterilizing-grade filters that provide sterility assurance, high flow rates and high throughput. They are used for sterile tank and gas venting, as well as for the filtration of liquids in small and large volume systems. Durapore 0.22 µm hydrophobic polyvinylidene fluoride (PVDF) membrane reliably eliminates contaminants and microorganisms in sterilizing applications, even at high pH.

Broad Chemical Compatibility, Low Extractables

Contributing to clean manufacturing processes, Durapore filters are made of just two materials—PVDF membrane and polypropylene support structure—this ensures broad chemical compatibility and low gravimetric extractables.

Regulatory Compliance

Filters with hydrophobic Durapore 0.22 µm membrane are designed, developed, and manufactured in accordance with a Quality Management System approved by an accredited registering body to an ISO® 9000 Quality Systems Standard and are shipped with a Certificate of Quality.

Each Opticap® XL capsule and Durapore cartridge filter is integrity tested during manufacturing and is supported with a comprehensive Validation Guide for compliance with regulatory requirements.

For traceability and easy identification, each filter is labeled with the product name and identifying characteristics.

Multiple Formats Available

Sterilizing-grade hydrophobic Durapore membranes are available in three formats and multiple configurations that vary by filtration surface area and type of inlet/outlet connection.

Membrane Types	Filter Formats
• Durapore 0.22 µm hydrophobic	• Opticap XL disposable capsule filters • Optiseal® cartridge filters • Cartridge filters

From process development to full-scale production, Millipore has the right solution for you!

Table of Contents

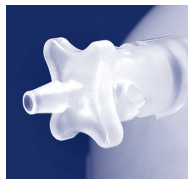
Opticap XL Disposable Capsule Filters

Opticap XL Filters

Opticap XL disposable capsule filters with hydrophobic Durapore membrane are available in multiple filtration areas, providing an optimal choice for every application. Each Opticap XL capsule is integrity tested during the manufacturing process. The Opticap XL capsule patented design allows unparalleled thermal and hydraulic stress resistance in a disposable filter, resulting in reliability, high confidence in the sterility process, and improved cleanliness. The unique capsule design with pleated hydrophobic Durapore membrane minimizes hold-up volume and reduces production losses.

Convenient and Easy to Use

Opticap XL capsule filters eliminate the time and expense associated with assembling, cleaning, and validating stainless steel housings. Adjustable, easy-to-turn upstream vents and drain valves with O-ring seals allow easy process control. Other ease-of-use features include flow direction arrows and ribbed housing for easy gripping, even with gloved-hands.



The Right Size

A wide range of filtration areas is available to fit all of your application needs, and to allow easy scale-up of your small volume filtration steps to larger, full-scale filtration processes.

The Right Connections

Self-contained, disposable Opticap XL capsule filters are supplied with a choice of inlet and outlet connections to optimize your filtration process. Connections include hose barb, fractional sanitary flange, and sanitary flange, which provide the highest flow rate.

Optiseal Cartridge Filters

Optiseal Filters

Featuring a unique cartridge-to-housing sealing mechanism and pleated membrane configuration, these Durapore 0.22 µm hydrophobic cartridges offer maximum sterility assurance. Each cartridge filter is integrity tested during the manufacturing process.

Cartridge Filters

Cartridge Filters

Hydrophobic Durapore cartridge filters provide high throughput and minimal differential pressure. Cartridges are robust, resilient, and designed to withstand multiple steam-in-place cycles. Each cartridge filter is integrity tested during the manufacturing process.

Durapore cartridge filters are available in five cartridge lengths, from five to thirty inches, and provide a full range of filtration areas to suit every size system. Three connection options are offered for easy adaptation to existing housings.

Specifications

	Opticap XL 5	Opticap XL 10
Nominal Dimensions		
Maximum length:	21.6 cm (8.5 in.)	33.5 cm (13.2 in.)
Body diameter:	10.7 cm (4.2 in.)	10.7 cm (4.2 in.)
Vent to vent diameter:	14.5 cm (5.7 in.)	14.5 cm (5.7 in.)
Filtration Area	0.35 m^2 (3.7 ft^2)	0.69 m^2 (7.4 ft^2)
Materials of Construction		
Filter membrane:	Hydrophobic PVDF	
Film edge:	Polypropylene	
Supports:	Polypropylene	
Structural components:*	Polypropylene	
Vent O-rings:	Silicone	
Vent/Drain	¼ in. hose barb with double O-ring seal	
Maximum Inlet Pressure	5.5 bar (80 psi) at 23 °C 2.8 bar (40 psi) at 60 °C 1.0 bar (15 psi) at 80 °C	
Maximum Differential Pressure		
Forward:	5.5 bar (80 psid) at ambient temperature,	1.0 bar (15 psid) at 80 °C
Reverse:	3.4 bar (50 psid) at ambient temperature	
Bubble Point at 23 °C	≥ 1170 mbar (17.0 psig) nitrogen with 70/30 IPA/water	> 1240 mbar (18.0 psig) nitrogen with 60/40 IPA/water
Nitrogen Diffusion	Through a water wet membrane at ambient room temperature at 1720 mbar (25 psig) nitrogen:	
	≤ 5 cc/min	≤ 10 cc/min
Bacterial Endotoxin	Aqueous extraction contains < 0.5 EU/mL as determined by the Limulus Amebocyte Lysate (LAL) Test.	
Bacterial Retention	Quantitative retention of 10^7 CFU/cm^2 *Brevundimonas diminuta* ATCC® 19146 per ASTM® methodology.	
Sterilization	May be autoclaved for 20 cycles of 30 minutes at 126 °C.	
Good Manufacturing Practices	These products are manufactured in a Millipore facility which adheres to FDA Good Manufacturing Practices.	
Non-Fiber Releasing	Durapore membrane meets the criteria for a "non-fiber releasing" filter as defined in 21 CFR 210.3 (b) (6).	
Component Material Toxicity	Component materials were tested and meet the criteria of USP <88> Reactivity Tests for Class VI Plastics. Durapore filters meet the requirements of the USP <88> Safety Test.	
European Pressure Equipment Directive	Millipore Corporation certifies that this product complies with the European Pressure Equipment Directive, 97/23/EC of 29 May 1997. This product has been classified under Article 3 § 3 of the Pressure Vessel Directive. It has been designed and manufactured in accordance with sound engineering practice to ensure safe use. In compliance with Article 3 § 3 of this Pressure Equipment Directive, this product does not bear the CE mark.	

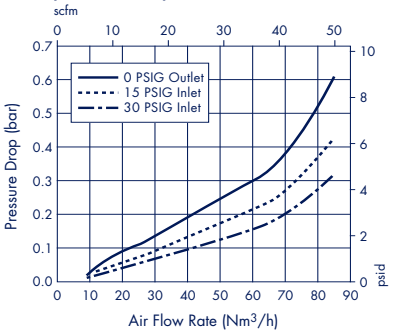
*Cage, core, end caps, and capsule housing

Specifications

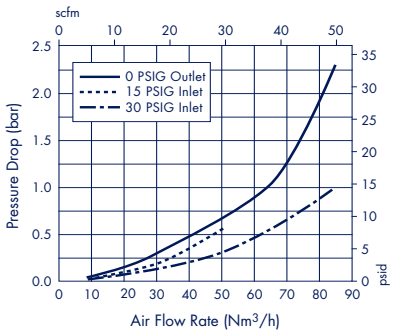
	Optiseal Filters	5-inch Cartridge	Per 10-inch Cartridge
Nominal Dimensions			
Maximum length:	12.0 cm (4.7 in.)	12.5 cm (5 in.)	25 cm (10 in.)
Outside diameter:	6.9 cm (2.7 in.)	6.9 cm (2.7 in.)	6.9 cm (2.7 in.)
Filtration Area	0.18 m^2 (1.9 ft^2)	—	0.7 m^2 (7.4 ft^2)
Materials of Construction			
Filter membrane:	Hydrophobic PVDF	Hydrophobic PVDF	
Supports:	Polypropylene	Polypropylene	
O-rings:	Silicone	Silicone	
Connections	Double 2-123 O-ring	Code 7 (2-226) O-ring with locking tab and spear Code 5 (2-222) O-ring with spear Code 0 (2-222) O-ring	
Maximum Differential Pressure			
Forward:	5.5 bar (80 psid) at 25 °C; 3.5 bar (50 psid) at 80 °C; 0.35 bar (5 psid) at 135 °C		
Reverse:	3.4 bar (50 psid) at 25 °C		
Bubble Point at 23 °C	≥ 2000 mbar (29 psig) in water ≥ 1240 mbar (18 psig) in 60/40 IPA/water ≥ 1170 mbar (17 psig) in 70/30 IPA/water	≥ 2000 mbar (29 psig) in water ≥ 1240 mbar (18 psig) in 60/40 IPA/water ≥ 1170 mbar (17 psig) in 70/30 IPA/water ≥ 1170 mbar (17 psig) in 100 IPA	
Nitrogen Diffusion	At 1.0 bar (15 psig) in 60/40 IPA/water at 23 °C: ≤ 2 cc/min At 1.7 bar (25 psig) in water at 23 °C: ≤ 5.0 cc/min	At 1.7 bar (25 psig) in water at 23 °C: ≤ 5.0 mL/min	≤ 10.0 mL/min
Bacterial Endotoxin	< 0.5 EU/mL as determined by the Limulus Amebocyte Lysate (LAL) Test.		
Bacterial Retention	Quantitative retention of *Brevundimonas diminuta* (ATCC 19146) following ASTM F838-83 methodology at a minimum challenge level of 10^7 CFU/cm^2.		
Sterilization	30 steam-in-place cycles of 30 min at 135 °C; 10 autoclave cycles of 30 min at 126 °C.	30 steam-in-place cycles at 30 min at 126 °C; 30 autoclave cycles of 60 min at 126 °C.	

Typical Air Flow Rate and Pressure Drop

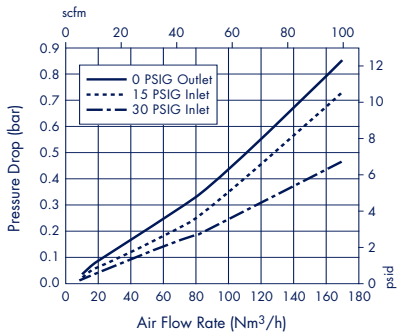
Opticap XL 5 Capsule with Hydrophobic Durapore 0.22 µm Membrane, FF Fitting*



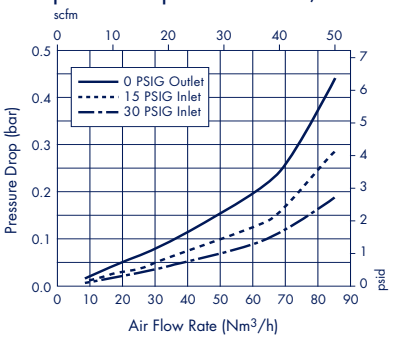
Opticap XL 5 Capsule with Hydrophobic Durapore 0.22 µm Membrane, HH Fitting*



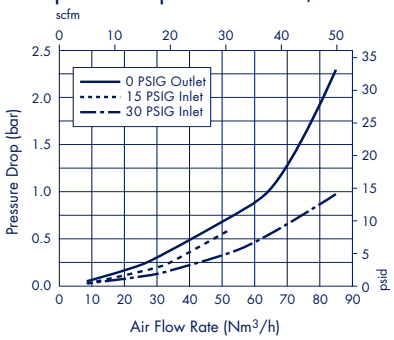
Opticap XL 5 Capsule with Hydrophobic Durapore 0.22 µm Membrane, TT Fitting*



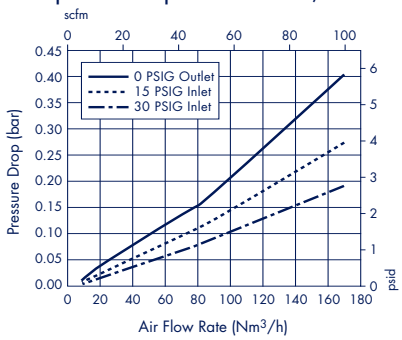
Opticap XL 10 Capsule with Hydrophobic Durapore 0.22 µm Membrane, FF Fitting*



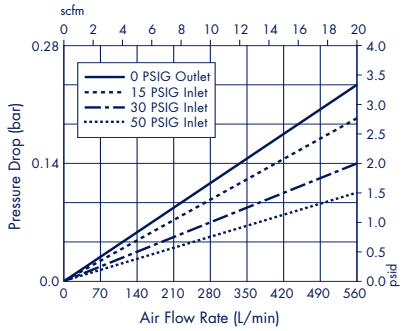
Opticap XL 10 Capsule with Hydrophobic Durapore 0.22 µm Membrane, HH Fitting*



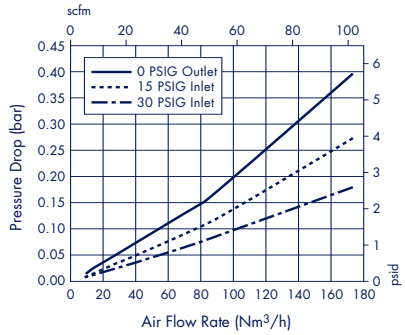
Opticap XL 10 Capsule with Hydrophobic Durapore 0.22 µm Membrane, TT Fitting*



Optiseal Cartridge with 0.22 µm Hydrophobic Durapore Membrane

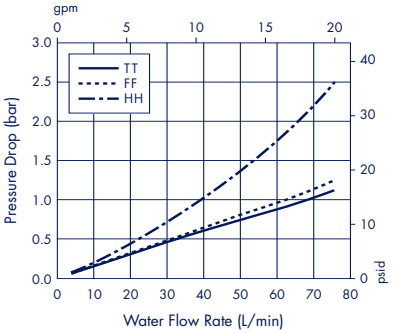


10-inch Cartridge with 0.22 µm Hydrophobic Durapore Membrane

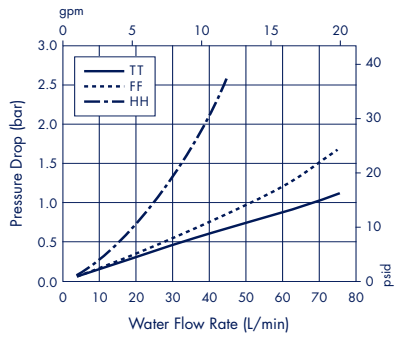


Typical Liquid Flow Rate and Pressure Drop

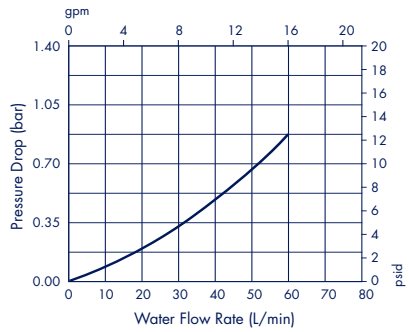
Opticap XL 5 Capsule with Hydrophobic Durapore 0.22 µm Membrane



Opticap XL 10 Capsule with Hydrophobic Durapore 0.22 µm Membrane



10-inch Cartridge with 0.22 µm Hydrophobic Durapore Membrane



***Opticap XL Capsule Connection Types**

TT = 38 mm (1½ in.) sanitary flange inlet and outlet; FF = 19 mm (¾ in.) sanitary flange inlet and outlet; HH = 14 mm (9⁄16 in.) hose barb inlet and outlet

Ordering Information

Device	Connections	Qty/Pk	Catalogue No.
Opticap XL 5 Capsules	38 mm (1½ in.) sanitary flange inlet and outlet	1/pk	KVGB A05 TT1
	19 mm (¾ in.) sanitary flange inlet and outlet	1/pk	KVGB A05 FF1
	14 mm (9⁄16 in.) hose barb inlet and outlet	1/pk	KVGB A05 HH1
Opticap XL 10 Capsules	38 mm (1½ in.) sanitary flange inlet and outlet	1/pk	KVGB A10 TT1
	19 mm (¾ in.) sanitary flange inlet and outlet	1/pk	KVGB A10 FF1
	14 mm (9⁄16 in.) hose barb inlet and outlet	1/pk	KVGB A10 HH1
Optiseal Cartridges	Double 2-123 O-ring	6/pk	LAGB 04T P6
5-inch Cartridges	Code 7 (2-226) O-ring with locking tab	1/pk	CVGB 75S 01
10-inch Cartridges	Code 7 (2-226) O-ring with locking tab and spear	3/pk	CVGB 71T P3
	Code 5 (2-222) O-ring with spear	3/pk	CVGB 51T P3
	Code 0 (2-222) O-ring	3/pk	CVGB 01T P3
20-inch Cartridges	Code 7 (2-226) O-ring with locking tab and spear	3/pk	CVGB 72T P3
	Code 5 (2-222) O-ring with spear	3/pk	CVGB 52T P3
	Code 0 (2-222) O-ring	3/pk	CVGB 02T P3
30-inch Cartridge	Code 7 (2-226) O-ring with locking tab and spear	3/pk	CVGB 73T P3
	Code 5 (2-222) O-ring with spear	3/pk	CVGB 53T P3
	Code 0 (2-222) O-ring	3/pk	CVGB 03T P3

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In every application, every step and every scale, count on Millipore to be everywhere for you—from monoclonals to vaccines, from clinical through pilot to full-scale manufacturing. Our technologies are used by most of the world's major biopharmaceutical companies. But we deliver more than advanced separation, purification, sterilization and quality control products. With Millipore, you get services to optimize and validate your processes, comprehensive resources to streamline and enhance your operation, unmatched know how forged from 50 years' experience—and solutions that integrate it all. For higher yields, improved process economics and faster speed to market, discover the more in Millipore.

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In the U.S., Canada and Puerto Rico, fax orders to
1-800-MILLIFX (1-800-645-5439)
Outside of North America contact your local office.
To find the office nearest you visit **www.millipore.com/offices.**
Internet: **www.millipore.com**
Technical Service: **www.millipore.com/techservice**

MILLIPORE

Lit. No. DS8932EN00 Rev. B 1/06 06-011

Products

> Dental Chair Unit
> Dental Suction Unit
> Central Air Suppl...
> Air Compressor
> Dental Curing Light

400-021-9236
021-60719286

Silent Oil Free Air Compressor

Model：GA-84

Power：3200W

Note:Powerful Air Compressor

Powerful Dental Air Compressor (piston type)
Model No.: GA-84
Brand: Greeloy (made in Shanghai, China)

Specification:
Power: 3200W (4pcs 800W motor)
Volt./Hz: 110~240V 50~60Hz
Speed: 1400/1750 r.p.m
Air Flow: 620L/min at 0Bar
Noise Level: 56dB
Max Pressure: 8Bar
Restart Pressure: 5Bar
Tank Capacity: 120L
Weight: 94/125kg
Product Size: 1105*450*645mm

Remark:
All Greeloy air compressors, can be with air dryer system & silent cabinet.

Advantages:
※ **Super silent.**
Low working noise, create a quiet working environment.
※ **Low vibration.**
With special rubberfeet, reduce vibration during operation.
※ **Pure air flow.**
Oil free design, no lubrication oil needed during operation.
※ **Core technology.**
Diamond hardness cylinder ensure durable working performance.
※ **Fashion and durable design.**
Compact structure, light weight. Under normal situation, can be used for more than 20000hours.
※ **Use safety.**
With multiple self protection system, if here will be abnormal with pressure, current or voltage, the motor would cut o
※ **Easy operation.**
Quite simple operation, connect to power supply, then no need any more maintenance, just drainage regularly.
※ **Low energy consumption.**
Full automatic design, automatic stop and restart control, low consumption.
※ **High precision filtration.**
With double filters, ensure high precision of outlet air flow.
※ **Tank inside has done anti-rust treatment.**
Ensure pure outlet air flow for medical equipments.

【打印】 【关闭】

Bio-Pharm

SANI-MATIC®

UltraFlow™: Powerful CIP in a Compact, Portable Design.

UltraFlow 110

UltraFlow 45

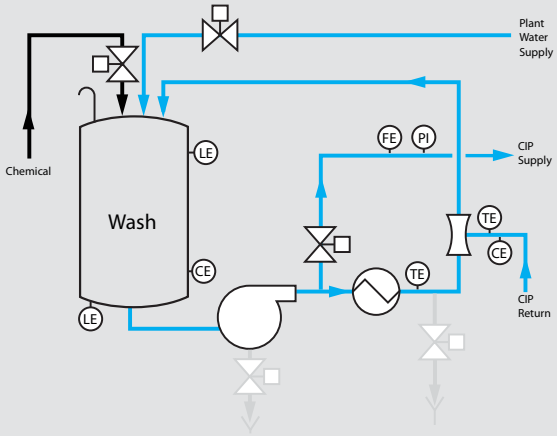
The Sani-Matic UltraFlow is a self-contained, compact and portable Clean-In-Place (CIP) System programmed to accommodate a variety of recirculated CIP applications. Designed for critical cleaning, the UltraFlow meets cGMP and ASME-BPE standards.

The Sani-Matic UltraFlow needs a mere 6 gallons of water to operate vs. conventional CIP Systems, which must maintain a significant quantity of water in the supply tank to prevent pump cavitation.

Advantages

- **Small Footprint.** Space-saving design for installations with limited floor space. Fits through standard doorways with ease.
- **Wide Operating Range.** The systems range from 2–45 gpm and 5–110 gpm and are able to clean small and large applications
- **Self-Cleaning.** Self-cleans without extra steps, and eliminates cross-contamination.
- **Portable.** Positioned on low-friction casters for easy movement between process suites. No expensive supply and return line installation required.
- **Water & Chemical Savings.** The high-turbulent flow rate and low water requirements for operation reduce the amount of water and chemicals needed for a complete clean.
- **Low Outlets? No Problem.** Returns solutions with entrained air to accommodate vessels with low and restricted outlets.

UltraFlow Schematic



Documentation

Standard

- Operation and maintenance manuals
- Recommended spare parts list
- Instrument list
- Instrumentation calibration procedures
- Performance data
- Material certificates
- Weld qualification and inspection records
- Inspection test results, reports and certificates
- Component catalog cut sheets
- As-built assembly drawings
- As-built process and instrumentation diagrams
- As-built electrical drawings
- PLC and HMI application files

Optional

- Functional Specifications (FS)
- Configuration Specification (CS)
- Factory Acceptance Test (FAT)
- Site Acceptance Test (SAT)
- Installation and Operation Qualification (IQ/OQ)
- Traceability matrix
- ISA data sheets
- Cleaning and passivation report
- Digital weld video record (Borescope)
- Printer
- Hydrostatic test certificate
- ASME data for heat exchanger
- Riboflavin coverage test

Features

UltraFlow 110

- 74" L x 33" W x 80" H (height may vary with options)
- Operating range of 5–110 gpm @ 60 psi
- Electric or steam heat
- For process tank diameters up to 10'
- For process line diameters up to 3"
- Mass flow meter

UltraFlow 45

- 68" L x 24" W x 74" H (height may vary with options)
- Operating range of 2–45 gpm @ 50 psi
- Electric or steam heat
- For process tank diameters up to 4.5'
- For process line diameters up to 2"
- Turbine flow meter

Standard for Both Models

- Wetted surface: 316L stainless steel, 25 Ra
  Non-wetted surface: 304 stainless steel, 32 Ra
- UL listed, 304 stainless steel, NEMA 4X enclosure
- Allen-Bradley CompactLogix
- Allen-Bradley PanelView Plus HMI
- Ethernet communication
- 40 customizable cleaning cycle programs
- Eductor return system
- A single centrifugal CIP supply pump
- Modulating diaphragm control valves to set cleaning circuit flow rates and to control the rate of discharge to drain
- Two chemical delivery systems comprised of pneumatic diaphragm pumps, removable chemical reservoirs
- Chemical conductivity, proof of rinse conductivity
- Supply and return temperature sensors
- Electric flow-through heater
- Discharge pressure gauge

Optional for Both Models

- 15 Ra Electropolish (EP) finish
- Allen-Bradley PanelView Plus 1000
- Printer
- Stainless steel motor
- Shell and tube heater
- Air blow manifold
- Chemical reservoir low level switches
- One chemical delivery system (standard offers two)
- One water supply valve (standard offers two)
- CIP supply routing valves
- Water connection bleed valves
- Sample valve
- Vent filter assembly
- Pressure transmitter
- Mass or turbine flow meter alternate
- Fixed position leveling feet
- Frame weld finish upgrade
- Sanitary flex hose package
- Piping insulation
- Fixed position seismic zone calculations
- Passivation
- Spare parts budget
- Larger electric heater
- Sani-Matic Start-up Services

Operating Requirements

UltraFlow 110

Instrument Air	½" NPT, 10 scfm @ 90 psi
Water Supply	Two 1" tri-clamps, WFI, DI, potable ≤ 2 gpm @ 25 psi, 20°–80° C
Drain	3" tri-clamp (programmable to meet app)
Dry Weight	1,400 lbs (approximate)
Electrical Power (with electric heat)	15 kW, 50 amps (standard) or 30 kW, 68 amps (optional) @ 460 VAC, 3 Ph, 60 Hz
Electrical Power (with steam heat)	27 amps @ 460 VAC, 3 Ph, 60 Hz
Plant Stream	1 ½" flange, 540 lbs/hr @ 50 psi
Plant Condensate	1" flange
CIP Supply	2" tri-clamp, 5–110 gpm @ 60 psi
CIP Return	3" tri-clamp, 5–110 gpm @ 11' of head @ 80° C
Vent/Overflow	2" tri-clamp

UltraFlow 45

Instrument Air	½" NPT, 10 scfm @ 90 psi
Water Supply	Two 1" tri-clamps, WFI, DI, potable ≤ 2 gpm @ 25 psi, 20°–80° C
Drain	2" tri-clamp (programmable to meet app)
Dry Weight	900 lbs (approximate)
Electrical Power (with electric heat)	12 kW, 27 amps (standard) or 24 kW, 43 amps (optional) @ 460 VAC, 3 Ph, 60 Hz
Electrical Power (with steam heat)	11 amps @ 460 VAC, 3 Ph, 60 Hz
Plant Stream	¾" flange, 195 lbs/hr @ 50 psi
Plant Condensate	½" flange
CIP Supply	1 ½" tri-clamp, 2–45 gpm @ 50 psi
CIP Return	2" tri-clamp, 2–45 gpm @ 8.5' of head @ 80° C
Vent/Overflow	2" tri-clamp

Cleaning Confidence.

Repeatable results you can count on every time you clean your process parts and equipment.
That's Cleaning Confidence from Sani-Matic.

SANI-MATIC®

sanimatic.com

Sani-Matic, Inc. 1915 S. Stoughton Rd., Madison, WI 53716 (p) 800-356-3300 (f) 608-222-5348

TSU™ Series -86°C Upright Ultra Low Temperature Freezers

Ensure ultimate protection and optimum capacity for your most critical samples with TSU™ Series –86°C Upright Ultra-Low Temperature Freezers.

Brand: Thermo Scientific TSU700V

Code : NEW

Additional Details : Weight : 411.00000kg

Description

- Choice of five capacities maximize sample storage while minimizing the freezer's physical space inside the lab
- High-performance mode provides the tightest temperature uniformity and peak variation†—for most applications, energy-savings mode offers excellent temperature control, plus up to 15% savings on energy usage compared to high performance mode
- Increases the internal capacity of 2 inch vials over previous generation freezers—gain up to 76% more capacity in the same footprint†— with 1mL CryBank tubes
- Five sizes accommodate any size lab, featuring the industry's leading capacity per footprint specifications‡
- Monitor the freezer's health 24/7 and access a detailed event log
- Obtain a record, simply download a report of the current event log to a portable drive
- Environmentally-friendly, CFC/HCFC free refrigerants
- High-efficiency compressors offer exceptional performance and reliability
- Brazed plate heat exchanger for more efficient heat transfer—induction brazed joints to reduce leak potential and improve reliability
- Power management system protects against a wide range of voltage variation and is easily accessible through the touch-screen display
- Remote alarm contacts compatible with external alarm and monitoring systems
- Two rear access, 1in. (25mm) ports allow for the use of inexpedient probes or instrumentation
- Store up to 15 years worth of temperature and event data on our on-board computer
- Use the new USB port to download freezer temperature and event log data, or freezer settings from one freezer to another
- Provides protection against dust on the condenser, which can cause reduced refrigeration performance and increased risk to samples
- Store up to 278 lbs. of samples (depending on freezer model) on our reinforced, stainless steel shelving
- 4×7 heated gasket provides four touchpoints of security and seven zones of protection, maximizing cabinet temperature and eliminating frost build-up
- Four polystyrene insulated inner doors help maintain cabinet temperature during openings and feature embedded rare earth magnets, eliminating exposed latches or magnets
- Several optional features including LN2 and CO_2 back-up system, chart recorder, stainless steel inventory racking solutions, and hands-free locking option

† Compared to energy-savings and high-prformance modes.

‡ Based on internal performance data; Data on file May 2011

Specifications

Amperage	9.5A
Hertz	50Hz
Insulation	Vacuum Panel and Water Blown Foam
Shipping Weight (Metric)	432kg
Backup Systems	CO2 or LN2 Optional
Access Security	KeyLock Standard, Padlock Compatible, Key Card Optional
Certifications/Compliance	cULus, CE listed
Description	Capacity: 33.5 cu. ft. (948.7L); Holds 700 boxes; 230V/50Hz
Dimensions (L x W x H) Exterior	37.6 x 49.2 x 78 in. (96 x 125 x 198cm)
Plug Type	European
Type	Ultra Low Freezer, Upright
Doors	Single
Electrical Requirements	230V 50Hz
Health Monitoring	On Screen, Log File
Inner Doors	4
Line Voltage Indicator	Line voltage and Buck/Boost
On-Board Datalogging	Standard

Display	Touch ScreenLCD
Holds	700 boxes
Shelves	3
Vial Capacity	70,000 x 2mL
Capacity (Metric) Shelf	432kg
Chart Recorder	7-day Ink or Inkless (Optional)
Data Outputs	RS-485, 4-20mA, dry contacts - standard
Capacity (Metric)	949L
Dimensions (D x W x H) Interior	28.3 x 40 x 51.2 in. (72 x 102 x 130cm)
Temperature Range	–50° to –86°C
Voltage	230V
Door Opening Recovery	39 min.
Energy Usage	18.5/21.8kW-hr/day
Footprint (Metric)	1.19 sq. meters
Interior	Painted Steel - Standard, Stainless-steel - Optional
Operating Modes	High Performance or Energy Efficiency
Peak Variation at -80C	+2.2/-5.5°C
Smart View Compatibility	Smart-Vue Compatible

Regulatory Approvals	CE
Setpoint Security	Standard - Individual user names and passwords
Vial to Footprint Ratio (Metric)	58.824 vials/cu. m
Warm up Time -80 C to -50C	241 min.
Water Cooled	Optional
Product Line	Thermo Scientific

Vial to Energy Ratio	1.31 watts/100mL vials (box)
Voltage Compensation	Buck/Boost
Weight (Metric)	432kg
Warranty	Warranty varies by country, please contact us for details

MWS

Water and Water/Glycol System

- **Heat Water and Water/Glycol Solutions to 300˚F (150˚C)**
- **50 - 800 kW**
- **240 V, 480 V and 600 V, 3 -Phase, 60 Hz**
- **Compact Footprint for Installation**
- **150# Welded Steel Construction**
- **Long Life 0.475 in. (12.1 mm) dia. Copper Sheath Heating Elements**
- **High Temperature Centrifugal Pump - rated to 300˚F (150˚C)**
- **Electronic Digital Temperature and Process Control**
- **Discharge Pressure Gauge**
- **UL NEMA 12 Electrical Enclosure Complete with Contactors, Temperature Safety Limit, Transformers and Pilot Light(s)**
- **External Cold Expansion Tank (Optional)**
- **External Heat Exchanger (Optional)**

Description

Chromalox MWS - Mid-Size Water/Glycol System - is engineered to operate to 300˚F (150˚C) with either water or water/glycol fluids. Its electric heating core assures responsive and precise temperature control in a space saving package. The system is suitable for a large range of heating needs with a compact design. The MWS operates in a closed loop system using a cold expansion tank (optional).

Applications

Chromalox MWS system is great for applications such as reactors, evaporators, dryers, platen presses, heat excangers, roll heating, or any jacketed kettles / vessels / tanks.

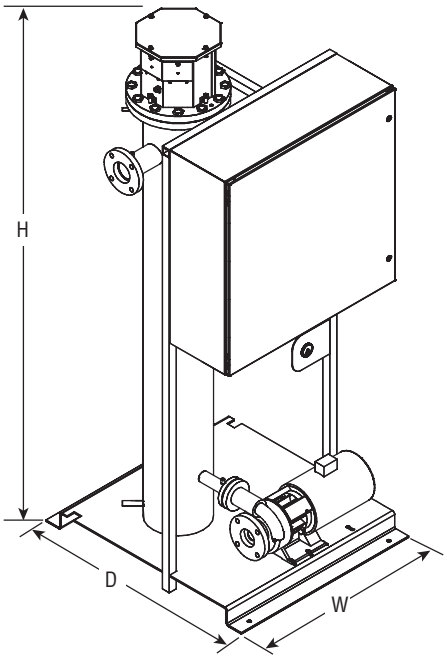
Hot water systems can be used in a variety of industries such as chemical, plastics, cosmetics, automotive, rubber, refining, pharmaceutical, non-woven / textiles/ fibers, aerospace, or any other industrial market.

Construction

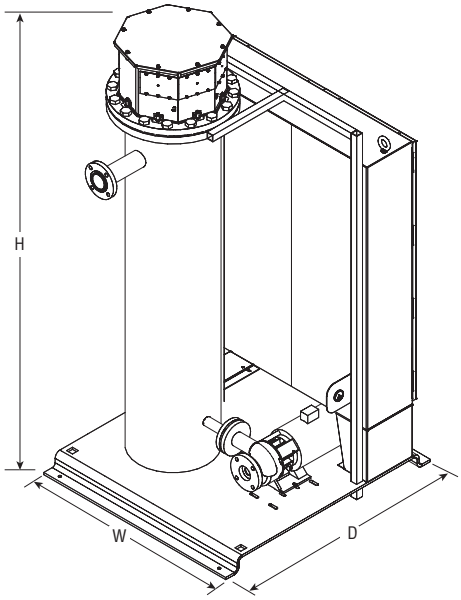
Chromalox MWS systems are ruggedly constructed for industrial applications. The heavy-duty, steel support base features channel grooves for forklift transport. The heater chamber is fully welded and houses Chromalox brand, long-lasting heating elements. The panel is fully UL-listed and assembled in-house. The pump is air-cooled with a mechanical seal, rated to 300˚F (150˚C). The final assembly is fully-shop tested prior to shipment.

WARNING — In hazardous areas, pipe surfaces could achieve temperatures high enough to cause auto-ignition of the hazardous material present. Consult Article 500 of the National Electric Code for further information on the maximum allowable temperature for a specific application.

MWS
Water and Water/Glycol System *(cont'd.)*



MWS 50-250 kW Unit (Front View)



MWS 300-600 kW Unit (Rear View)

Options

- Electronic Solid State (SCR) Trim Power Control
- Strainer
- Powder Coated or Stainless Steel Side Coverings
- Dedicated Fill Connection
- NEMA 4 or 4X (Stainless) Construction
- Class 1, Div 2 Hazardous Area Rating (with purge)
- Panel Disconnect Switch
- Heater On/Off Switch
- Suction Pressure Guage
- Inlet / Outlet 150# Gate Valves
- Drain / Bleed Values
- Digital Overtemperature Controller
- Relief Valve
- ASME Design & Certified, Section VIII, for 100 psi (7 bar) at 300˚F (150˚C)
- High Flow Pump (300 GPM, 450-800 kW only)
- Heat Exchanger (shipped loose for customer installation)
- Expansion Tank (shipped loose for customer installation)
- Liquid Level Switch for Expansion Tank

Unit Proportions

Unit Size	Weight (Lbs.)	Width (In.)	Depth (In.)	Height (In.)	Flow Rate[1] GPM	Pressure[1] TDH	Motor HP	Inlet/Outlet Connection	System Capacity (Gal.)
50 - 150 kW	900	36	42	96	60	100	3	2", 150#	25
175 - 250 kW	1400	36	42	96	120	100	5	3", 150#	35
300 - 400 kW	2000	48	54	96	200	100	10	3", 150#	55
450 - 600 kW	2600	48	54	96	200[2]	100[2]	10[2]	3", 150#[2]	65
650 - 800 kW	3600	61	54	99	200[2]	100[2]	10[2]	3", 150#[2]	85

[1] Refer to Pump Graph in instruction manual for full operating range.
[2] Option for 300 GPM 15 HP pump with 4", 150# inlet/outlet.

Standard Features — *Benefits*

Electronic Process Control ..... Precise process control
Element Overtemperature Protection ..... Protect elements and fluid from overheating
Air-Cooled Mechanical Seal ..... No external cooling needed
Insulated Heating Chamber ..... Maximize efficiency by minimizing heat loss
Discharge Pressure Gauge ..... Confirm pump operating performance
Compact Footprint ..... Space saving design
Fully Pre-wired & Tested ..... Ready to operate on site
Centrifugal Pump ..... Minimize piping configuration
Temperature rating to 300˚F (150˚C) ..... Covers most applications
150# ANSI Flange Connection ..... Easy fit up to installed piping
Start / Stop buttons with Motor Starter ..... Complete operating system
Pilot Lights for Power, Heater, & Pump ..... Visual indication of system operation

MWS

Water and Water/Glycol System *(cont'd.)*

Ordering Information

To Order — Complete the Model Number using the Matrix provided.

MWS — Mid-Size Water and Water Glycol System

Unit Temperature Rating[1]

Code	
300	300˚F (150˚C)

Kilowatts

50	50 kW	**150**	150 kW	**300**	300 kW	**550**	500 kW
75	75 kW	**175**	175 kW	**350**	350 kW	**600**	600 kW
100	100 kW	**200**	200 kW	**400**	400 kW	**800**	800 kW
125	125 kW	**250**	250 kW	**500**	500 kW		

Enclosure Types

Code	
E1	General Purpose
E4	Moisture Resistant
E4X	Moisture / Corrosion Resistant (Stainless Steel)
E4NP	Class 1, Div 2 rating - Nitrogen Purge (by customer)

Option

Code	
(Blank)	No Options
ST	SCR Trim
SR	Strainer[2]
GV	I/O Gate Valves[2]
FC	Dedicated Fill Connection[2]
DB	Drain / Bleed Valves
PD	Panel Disconnect
HW	Heater On/Off Switch
SG	Suction Pressure Guage
DT	Digital Overtemp Control
SV	Safety Relief Valve - 125psi
PC	Power Coated Skins
SS	Stainless Skins
AE	ASME Designed & Certified
HF	300 GPM Pump[3]
XX	Custom Feature

Voltage

Code	
240	240 V (only available for 50 and 75 kW units)
480	480 V
600	600 V

Phase

Code	
3P	Three-Phase

Kilowatts

Code	
150	kW

MWS	- 300	- 150P	- E4	GV	480V	3P	150kW	Typical Model No.

Example of Final Model Description: MWS-300-150P-E4GV 480V 1-3P 150kW

[1] Unit operating temperature based on 104°F (40°C) max. ambient, indoor invironment

[2] When ordering more than one of these options, some items will be shipped loose to avoid damage during shipment. Simple assembly will be required for installation.

[3] 300 GPM option comes with 15 HP motor and 4", 150# inlet/outlet connections.

Cert. No. LRQ 0963008
ISO 9001

CSM-K
High Capacity Clean Steam Generator

The typical package shown below is for illustration purposes only

Description

The CSM-K range of high capacity clean steam generators has been designed to provide sterilizer grade clean steam from suitably treated feedwater using plant steam as the heating medium. Units using other fluids on the heating media can be provided to special order.

The range covers outputs up to 3800 kg/h.

The pressure vessel is manufactured in accordance with PED 97/23/EC and is supplied with a standard package of documentation. The primary medium passes through a tube bundle which can be extracted for cleaning and maintenance. All secondary wetted parts are manufactured from 316 stainless steel.

Applications

Suitable for process applications, laundries, food and beverage applications, hospital sterilizers, laboratories and humidification. The CSM-K can also be used in a number of electronic production processes, pharmaceutical and general biotechnological applications. Please refer to our general sales brochure on clean steam for information on other products that can be used in association with the clean steam generator.

Principle features:

- Produces clean steam for sterilization, humidification, and culinary or clean processes, from standard plant steam.
- Fully assembled skid-mounted with all essential safety systems.
- PLC for accurate steam and feedwater pressure control.
- All clean steam wetted parts in 316 stainless steel to avoid contamination.
- Produces steam to HTM 2031 standards.
- Automatic blowdown controls - TDS and bottom blowdown.

Materials

Primary steam header	Carbon steel
Primary side pipework and fittings	SG iron and carbon steel
Tube sheet	Stainless steel AISI 316L
Gaskets	Reinforced graphite
Tube bundle	Stainless steel AISI 316L
Shell	Stainless steel AISI 316L
Shell side flanges	Stainless steel AISI 316L
Support frame	Carbon steel
Insulation (optional extra)	Rock wool + Cover in Aluminium (standard) or stainless steel 304

Maximum steam pressures

Maximum primary steam pressure	12 bar g
Maximum clean steam pressure	7 bar g

Local regulations may restrict the use of this product to below the conditions quoted.
In the interests of development and improvement of the product, we reserve the right to change the specification without notice.

Technical data

Pneumatics	**Compressed air:** A 6 bar g compressed air supply is required; where this is unavailable an optional compressor can be supplied with the unit (at extra cost).
Electrical	**Electrical requirements:** 400 V 3-phase 50 Hz. A fused isolator of the correct rating must be incorporated in the supply line as near as possible to the unit. Information on the installed load for each individual unit will be supplied by Spirax Sarco.
Feedwater quality	To meet the requirements of HTM 2031 we would recommend the use of de-mineralised or reverse osmosis feedwater. It is advised that analysis of the feedwater is undertaken prior to installation and commissioning. Whilst not mandatory the table opposite gives a guide to recommended typical values.
Control	The unit is PLC controlled with the generator having pressure and level control.

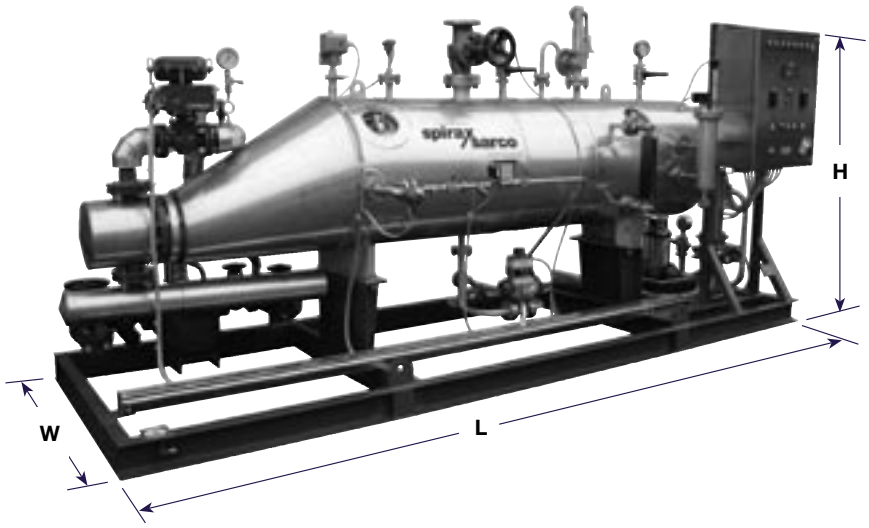
Property	Maximum value
Ammonium	0.2 mg/l
Heavy metals substitute	0.1 mg/l
Chloride	0.5 mg/l
Nitrate	0.2 mg/l
Residue on evaporation	30.0 mg/l
Phosphate	0.1 mg/l
Silicate	0.1 mg/l
Electrical conducivity at 25°C	35.0 µS/cm

Dimensions (approximate in mm) and standard output production (approximate in kg/h)

Standard output production is based on the following conditions:
- Primary steam pressure 10 bar g;
- Clean steam pressure 3.5 bar g;
- Feedwater inlet temperature 20°C

Engineering drawings, including holding down details, will be provided after ordering 'for approval' and as 'final certified' (as built).

Model CSM-K		401	402	403	501	502	503	601	602	603	604	702	703	704	802	803	804
Maximum dimensions (guidance) in mm	Length **L**	2900	3400	3700	3000	3500	3800	3300	3800	4000	4750	3900	4150	4900	4000	4000	5000
	Width **W**	1400	1400	1400	1500	1500	1500	1700	1700	1700	1700	1800	1800	1800	1900	1900	1900
	Height **H**	1600	1600	1600	1700	1700	1700	1900	1900	1900	1900	2050	2050	2050	2250	2250	2250
Clean steam output (kg/h)		260	320	370	500	620	700	930	1150	1300	1700	1730	2000	2630	2600	2900	3800



Sizing and selection

For further information, please refer to TI-P486-13.

Typical specification

The clean steam provider shall be a Spirax Sarco clean steam generator CSM-K704 designed and built to produce steam to the HTM 2031 standard, dependant upon feedwater.
To raise 2000 kg/h of clean steam at 3 bar g when supplied with plant steam at 8 bar g.
All items are to be pre-assembled and mounted on to a compact frame.

How to order

Example: 1 off Spirax Sarco CSM-K704 clean steam generator.
Please provide details of primary steam pressure, clean steam pressure, clean steam flowrate and feedwater system.

Ancillary items to be used depending on installation:
- Blowdown vessel and system.
- Clean steam check valves.
- Clean steam isolation valves.
- Primary steam isolation valves.
- Clean steam and primary steam trapsets.
- CSM-PD preheater and degasser unit.

Other items may be required, please contact Spirax Sarco to discuss the full installation.

Telstar® Puretech™

WFIS

Water For Injection Stills

WFIS
Water For Injection Stills

A choice of quality

Telstar Puretech Multiple Effect Water for Injection Stills are designed and constructed to produce pyrogen-free sterile water (WFI) in full compliance with cGMP guidelines as per FDA and EMEA requirements.

Engineering and manufacturing practices follow ISO 9001 procedures, ASME BPE criteria, GAMP guidelines, etc. Design and construction meets the most stringent Regulations and Codes from Europe, USA and others concerning safety and pressure vessels.

To ensure the equipment meets your requirements, we work in partnership with you and a dedicated team follows your order as a unique project. We develop specific Quality Plans (DQ, IQ and OQ) and undertake factory acceptance testing (FAT) to give assurance, performance and quality.

WFI applications

WFI water for injection, as defined in the Ph Eur and the USP, is used for the preparation of medicines for injectable administration, where water is used as a vehicle (water for injections in bulk), to disolve or dilute substances or preparations for injectable administration before use (sterile water for injections). According to the Ph. Eur water for injections can only be produced by distillation, of drinking water or purified water.

Design & construction features

Compact and Modular

The unit and all its components such as feed water pump, pre-heater and condensers are mounted on a stainless steel AISI 304 skid.

All parts in contact with the media are made of stainless steel AISI 316L, insulated with mineral wool (asbestos-free material) with external cladding made of stainless steel AISI 304. Inner surfaces are polished to Ra ≤ 0.64 µm and electro polishing is an available option.

Hygienic design: Including clamp connections, orbital welding techniques for tubing and components, minimisation of dead legs and proper piping slopes for self-drainability, double tube sheet construction in first column, condenser and pre-heaters, diaphragm valves for distillate/reject, etc.

Simple and Efficient Design

The lower part of the column consists of a double tube sheet shell heat exchanger with a large central pipe surrounded by a bundle of peripheral seamless pipes. This arrangement produces a natural fluid circulation: ascendant inside the peripheral pipes and descendant inside the central one. Steam flows up very slowly but droplets cannot reach the top of the column as they fall down simply by gravity. Thus, impurities such as particles and pyrogens contained in the droplets are dragged down towards the bottom of the column where they are automatically blown down. Pure steam from the first column serves as heating energy in the next column where it condenses as WFI. This can be reproduced several times, so called multiple effects, up to 7 columns. The more effects we install, the less heating energy and cooling water required.

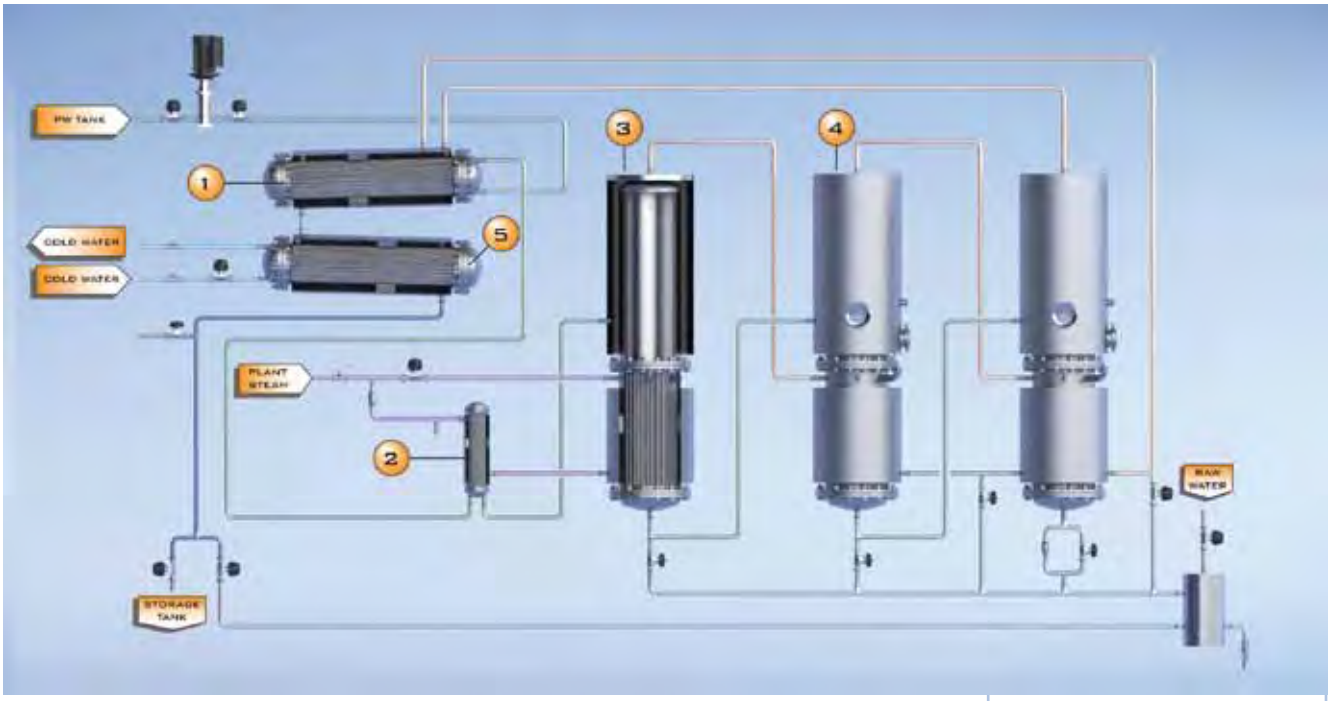
Ease of Maintenance and Installation

The heat exchangers are totally accessible and no internal elements are located within the column. This makes inspection much easier than other designs, with long pipes or internal heat exchangers.

The replacement of column gaskets can be done easily and quick, without needing to dismantle the column, which removes the need for very high technical areas in order to take off any internal part.

Heat exchanger pipes are always totally immersed in water, so there is a very low tendency to build up scale inside the tubes. Moreover, as they are shorter than other designs, they are less stressed by vibrations and risk of corrosion is significantly reduced.

Operating principle



Feed water (PW) is pre-heated by means of two DTS heat exchangers, which use respectively the heat of the pure steam and distillate water outlet and the plant steam outlet. The first column of the CS water still is equal to our CPS steam generators, heated also with plant steam.

The pure steam produced in the first column is used as the heating medium for the next one, so it condenses and turns into WFI. Simultaneously, the partial amount of non-evaporated water goes to the next column, so it is also partially evaporated as pure steam and used as heating energy for the next column.

Here, the pure steam also condenses (resulting in WFI distillate) and it is transferred by pressure to the successive columns.

1. **DTS PRE-HEATER**
2. **DTS HEAT EXCHANGER**
3. **PLANT STEAM HEATED COLUMN**
4. **PURE STEAM HEATED COLUMN**
5. **CONDENSER**

Control system

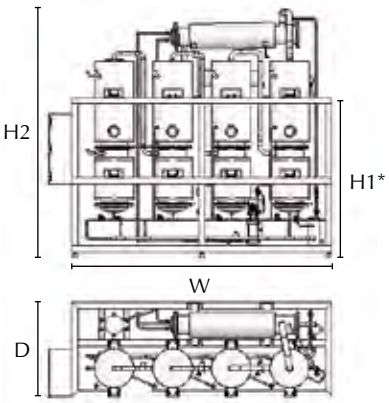
The control system is based on a PLC wire operator supervision via a user-friendly touch-screen HMI with the following menu:

- Mimics of the equipment, showing the operational state in real time
- Process parameters (temperature, pressure and conductivity)
- Setting up of parameters
- Alarm information
- Start-up and alarm recognition.

Options include: paper or electronic chart recorder for pure steam conductivity, temperature, extra feed water conductivity meter, on-line TOC monitoring, etc.

Technical data

MODEL	No. of effects	Overall dimmensions				Main Utilities			Approx. Weight Kg
		Width (W) mm	Height (H1) mm	Height (H2) mm	Depth (D) mm	Distillate output l/h	Heating steam @ 8 bar kg/h	Cooling water (25-50º C) l/h	
WFIS 3-250	3	2.140	2.000	2.900	1.300	270	130	1.095	800
WFIS 3-500	3	2.105	1.900	2.875	960	500	235	2.030	1.000
WFIS 4-500	4	2.500	1.900	2.875	960	500	190	1.185	1.200
WFIS 4-750	4	2.910	2.100	3.100	1.100	775	295	1.835	1.350
WFIS 4-1250	4	3.040	2.230	3.090	1.180	1.200	460	2.840	1.500
WFIS 5-500	5	2.915	1.900	2.875	960	500	165	650	2.100
WFIS 5-750	5	3.420	2.100	3.070	1.100	775	255	1.005	2.300
WFIS 5-1250	5	3.590	2.230	3.090	1.180	1.200	390	1.555	2.500
WFIS 5-2000	5	3.700	2.400	3.550	1.500	2.075	680	2.690	3.000
WFIS 5-3000	5	4.200	2.685	3.830	1.500	3.065	1.000	3.970	3.400
WFIS 5-4500	5	4.400	2.950	3.975	1.600	4.585	1.500	5.940	3.800
WFIS 6-2000	6	4.270	2.400	3.550	1.500	2.075	605	1.150	4.200
WFIS 6-3000	6	4.880	2.980	3.830	1.500	3.065	890	1.695	4.700
WFIS 6-4500	6	5.315	2.950	3.975	1.548	4.585	1.335	2.540	5.200
WFIS 6-6500	6	5.900	3.080	4.420	1.630	6.535	1.900	3.615	5.800
WFIS 6-9000	6	6.900	3.080	4.420	1.800	9.060	2.635	5.015	6.500
WFIS 6-12000	6	6.675	3.170	4.500	2.100	12.640	3.680	11.665	7.200
WFIS 7-3000	7	5.560	2.980	3.830	1.500	3.065	815	0	6.000
WFIS 7-4500	7	6.050	2.950	3.975	1.550	4.585	1.220	0	7.400
WFIS 7-6500	7	6.710	3.080	4.420	1.630	6.535	1.740	0	8.800
WFIS 7-9000	7	7.510	3.080	4.420	1.800	9.060	2.410	0	10.300
WFIS 7-12000	7	7.700	3.170	4.500	2.400	12.645	3.365	0	12.500



** WFIS OUTLET*

Options and accessories

- Feed water conductivity monitoring
- Pure steam take from the first column
- Elevated WFIS condenser
- Hot standby mode
- Sanitisation/Sterilization of the separator columns and WFIS condensers
- Protective mesh guarding
- On-line TOC monitoring device
- WFI storage and distribution skid.

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ISO 9001: Certified Company

BR-WFI-EN-1110

Data Sheet

Millistak+® Pod disposable depth filter system

Innovative, High-Performance Pod Filters are ideal for Primary and Secondary Clarification in Lab, Pilot and Process-Scale Applications.

Millistak+® depth filter media is offered in a scalable, disposable format, the Pod Filter System. Accommodating applications from lab to pilot to process scale, the Pod format offers greater flexibility because of its unique modular and 100% disposable design.

The Millistak+® Pod system is ideal for a wide variety of primary and secondary clarification applications, including cell cultures, yeast and *E. coli* lysates post centrifuge, *E. coli* refolds, media, vaccines, plasma proteins and sera.

Millistak+® Pod filters are available in three distinct series of media grades in order to meet your specific application needs. Millistak+® DE, CE and HC media deliver optimal performance through a gradient density matrix as well as positive surface charge properties.

Benefits

- Low hold-up volume for greater product yield
- Broad range of media types offered in single and multilayer products
- Millistak+® HC dual-action media improves prefiltration and compresses clarification
- Flexible, modular format offers scalability from 5 to 12,000 liters or more
- Patented disposable design eliminates need for housing, CIP or cleaning validation
- Self-contained Pod filters protect operators from exposure to biohazards
- Robust construction is easy to use and set up
- Smaller footprint facilitates use in tight spaces

EMD Millipore Corp. is a subsidiary of Merck KGaA, Darmstadt, Germany

Linear Scalability

The innovative Pod filter system consists of eight filter sizes and two expandable holders. No matter what size Pod filter you choose, the same flow path and configuration ensures a linearly scalable solution from bench to process scale.

Easy to Use

With the compact, modular design of our Pod system, you can increase productivity and shorten cycle times.

Installation and set-up of the Pod system is simple and straightforward. The unique design of the disposable adapters and disposable manifolds makes it easy to connect the Pod filters to the rest of the unit operations in the process. The self-contained and disposable nature of the system protects operators from exposure to biohazards and eliminates maintenance as well as cleaning validation requirements.

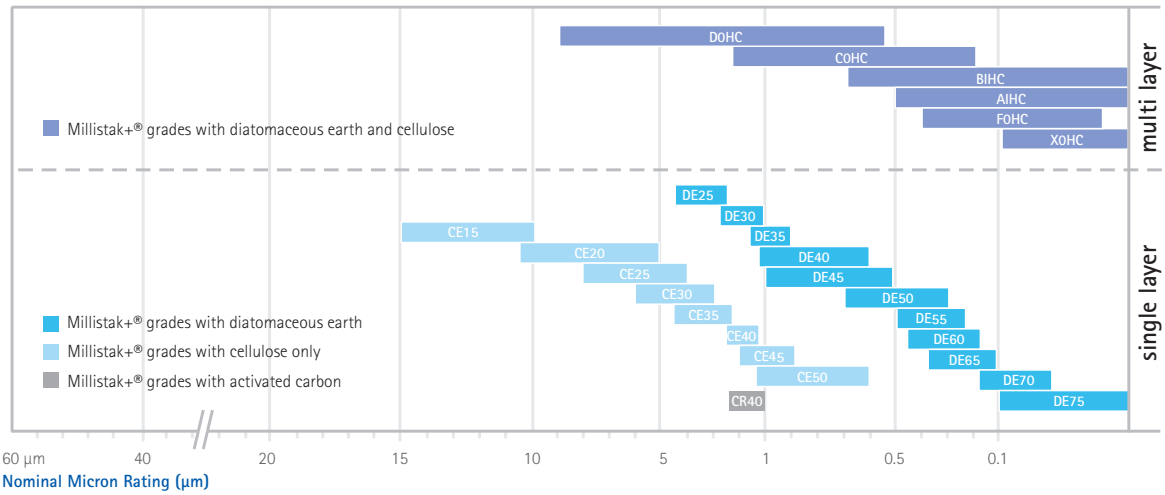
Configurations

- µPod® filter – 23 cm^2
- Lab scale Pod filter – 0.027 m^2, 0.054 m^2
- Millistak+® DE and CE media – 0.11 m^2, 0.77 m^2, or 1.4 m^2 filtration area.
- Millistak+® HC media – 0.11 m^2, 0.55 m^2, or 1.1 m^2 filtration area.
- Process scale holder – accepts from five to ten Pod filters per rack. Up to three racks can be stacked for process flexibility.
- Pilot scale holder – accommodates up to two full size Pod filters for configurations from 0.11 m^2 to 2.8 m^2 depending on media type. An optional accessory kit expands capacity to five full scale Pod filters.
- Disposable adapters – connect Pod filters to process piping, creating disposable flow path.
- Disposable diverter plates – enable more than one media grade on a single rack

Millistak+® Depth Filter Media

Available in three media series, the proven filtration performance of Millistak+® filter media in the Pod format provides greater flexibility and reduced cycle times. Millistak+® Pod filters incorporate multiple graded-density layers and adsorptive, positively-charged filter media. Composed of select grade cellulose fiber and diatomaceous earth, the Millistak+® DE series not only improves the manufacturing process, but also increases contaminant holding. In addition, the Millistak+® CE series consists of single layer media with cellulose fibers that are suitable for coarse filtration applications.

Millistak+® HC series improves productivity by combining multiple media grades into one device enabling compression of multiple filtration stages downstream of the bioreactor.



Typical Extractables

	Single Layer Millistak+® CE & DE Media	Millistak+® HC Media (non X0HC)	Millistak+® X0HC/F0HC Media
Conductivity	1.52 - 1.94 µS/cm post autoclave (1 cycle of 60 minutes at 123 °C) and pure water flush of 5 L/ft² (50 L/m²) of media surface area	3.64 - 10.5 µS/cm post autoclave (1 cycle of 60 minutes at 123 °C) and pure water flush of 10 L/ft² (100 L/m²) of media surface area	19.34 - 53.2 µS/cm (X0HC) and 21.4 - 42.7 µS/cm (F0HC) post autoclave (1 cycle of 60 minutes at 123 °C) and pure water flush of 10 L/ft² (100 L/m²) of media surface area
NVR Gravimetric Extractables	Not Tested	420 - 750 mg/f² (process scale) and 630 - 1251 mg/m² (lab-scale) per 24 hour static soak in pure water (type 1 DI water) post autoclave (1 cycle of 60 minutes at 123 °C) and pure water flush of 10 L/ft² (100 L/m²) of media surface area	Not Tested
TOC	910 - 1800 ppb post autoclave (1 cycle of 60 minutes at 123 °C) and pure water flush of 5 L/ft² (50 L/m²) of media surface area	720 - 4600 ppb post autoclave (1 cycle of 60 minutes at 123 °C) and pure water flush of 10 L/ft² (100 L/m²) of media surface area	1200 - 2800 ppb (X0HC) and 460 - 3200 ppb (F0HC) post autoclave (1 cycle of 60 minutes at 123 °C) and pure water flush of 10 L/ft² (100 L/m²) of media surface area

Metals (mg/ft² Media)	DE Series	CE Series	A1HC Series	X0HC Series	F0HC Series
Sodium	≤ 11.5	≤ 9.91	≤ 38.2	≤ 14.02	≤17.313
Calcium	≤0.050	≤ 1.46	≤ 7.30	≤ 9.60	≤5.170
Potassium	≤0.351	≤ 0.042	≤ 1.18	≤ 0.82	≤0.439
Magnesium	≤ 0.129	≤ 0.662	≤ 2.31	≤ 3.905	≤1.464
Iron	≤ 0.042	≤ 0.042	≤ 0.090	< 0.001*	<0.041
Lead	≤ 0.0004	≤ 0.0004	<0.001	<0.001*	<0.001
Aluminum	≤ 0.025	≤ 0.059	≤ 0.141	≤ 0.084	≤0.021
Titanium	<0.001*	<0.001*	≤0.019	≤ 0.04	<0.001
Chromium	≤0.001	0.0003	≤0.003	≤0.001	<0.001
Manganese	≤0.001	≤0.001	≤ 0.487	≤ 0.425	≤0.370
Cobalt	≤0.0002	0.0002	≤0.002	≤0.001	≤0.002
Nickel	≤0.001	≤ 0.0004	≤0.013	≤ 0.013	≤0.022
Copper	≤0.003	≤ 0.0004	≤ 0.167	≤ 0.009	≤0.019
Zinc	≤0.002	≤ 0.003	≤0.112	≤ 0.046	≤0.052
Mercury	≤ 0.0004	≤ 0.0004	<0.001*	<0.001*	<0.001
Arsenic	≤0.003	≤ 0.002	≤ 0.011	≤ 0.009	≤0.004

*Pilot and process scale only

Small Scale:
HC, DE, CE: 23 cm²

Lab Scale:
HC, DE, CE: 270 - 540 cm²

Pilot Scale:
HC: 0.11 - 5.5 m²
DE or CE: 0.11 - 7.1 m²

Process Scale:
HC: 5.5 - 33 m²
DE or CE: 7.1 - 43 m²

Millistak+® Pod Filter Specifications

Surface Area	23 cm^2 (HC, CE and DE media)	1.2 ft^2 (0.11 m^2) (HC, CE and DE media)	5.9 ft^2 (0.55 m^2) (HC media)	8.3 ft^2 (0.77 m^2) (CE and DE media)	11.8 ft^2 (1.1 m^2) (HC media)
Materials of Construction					
Filter Media:	Cellulose fibers with inorganic filter aid (CE Media contains cellulose only)				
Filter Membrane:	Mixed esters of cellulose (grades A1HC and B1HC only)				
Pod Housings:	Glass Filled Polypropylene				
Adapters:	Glass Filled Polypropylene*				
Gaskets and Plugs:	Thermo Plastic Elastomer (TPE)*				
Inlet, Vent and Outlet Connections	Female Luer			Flat seal	
Pod Dimensions					
Length:	3.5 in. (8.9 cm)	24.2 in. (62 cm)	24.2 in. (62 cm)	24.2 in. (62 cm)	24.2 in. (62 cm)
Height:	2.6 in. (6.6 cm)	12.5 in. (32 cm)	12.5 in. (32 cm)	12.5 in. (32 cm)	12.5 in. (32 cm)
Thickness:	1.6 in. (4.1 cm)	1.2 in. (3 cm)	2.8 in. (7.1 cm)	3.1 in. (7.9 cm)	4.8 in. (12.2 cm)
Maximum Operating Pressure	50 psig (3.5 bar) at ≤40° C		50 psig (3.5 bar) at 25 °C; 15 psig (1.0 bar) at 80° C		
Maximum Differential Pressure					
Forward:	30 psid (2.1 bar) at 40 °C		30 psid (2.1 bar) at 25° C; 15 psid (1.0 bar) at 80° C		
Reverse:	15 psid (1.0 bar) at 40 °C		30 psid (2.1 bar) at 25° C		
Sterilization	2 cycles of 60 minutes at 123° C		1 cycle of 60 minutes at 123° C		
Indirect Food Additive	All components meet the FDA indirect food requirements cited in 21 CFR 177-182.				
Toxicity	All component materials meet the requirements of the current USP <88> biological reactivity test for class VI plastics.				
Bacterial Endotoxin	< 0.25 EU/mL as determined by the Limulus Amebocyte Lysate (LAL) test.				
CE Pressure	This filter has been designed and manufactured according to the essential requirements of the Pressure.				
Equipment Directive	Equipment Directive 97/23/EC. Only 0.77 m^2, 1.1 m^2 and 1.4 m^2 filters carry the CE mark.*				

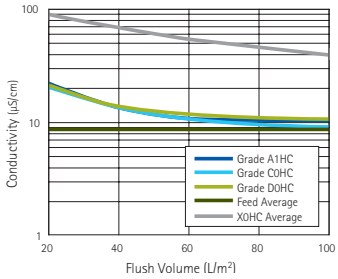
* Pilot and process scale only.

Millistak+® Pod Filter Specifications

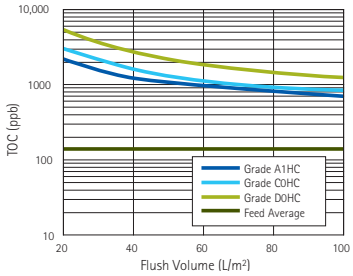
Surface Area	15.4 ft^2 (1.4 m^2) (CE and DE media)	0.29 ft^2 (0.027 m^2)	0.58 ft^2 (0.054 m^2)
Materials of Construction			
Filter Media:	Cellulose fibers with inorganic filter aid (CE Media contains cellulose only)		
Filter Membrane:	Mixed esters of cellulose (grades A1HC and B1HC only)		
Pod Housings:	Glass Filled Polypropylene		
Adapters:	Glass Filled Polypropylene*		
Gaskets and Plugs:	Thermo Plastic Elastomer (TPE)*		
Pod Dimensions			
Length:	24.2 in. (62 cm)	8.5 in. (22 cm)	8.5 in. (22 cm)
Height:	12.5 in. (32 cm)	5.3 in. (14 cm)	5.3 in. (14 cm)
Thickness:	5.0 in. (12.7 cm)	2.9 in. (7.9 cm)	3.7 in. (9.4 cm)
Maximum Operating Pressure	50 psig (3.5 bar) at 25 °C; 15 psig (1.0 bar) at 80 °C	30 psig (3.5 bar) at 37 °C	
Maximum Differential Pressure			
Forward:	30 psid (2.1 bar) at 25 °C; 15 psid (1.0 bar) at 80 °C	30 psid (2.1 bar) at 4-37 °C	
Reverse:	30 psid (2.1 bar) at 25 °C	30 psid (2.1 bar) at 37 °C	
Sterilization	May be autoclaved for 1 cycle of 60 minutes at 123 °C	2 cycles of 60 minutes at 123 °C	
Indirect Food Additive	All components meet the FDA indirect food requirements cited in 21 CFR 177-182.		
Toxicity	All component materials meet the requirements of the current USP <88> biological reactivity test for class VI plastics.		
Bacterial Endotoxin	< 0.25 EU/mL as determined by the Limulus Amebocyte Lysate (LAL) test.		
CE Pressure	This filter has been designed and manufactured according to the essential requirements of the Pressure		
Equipment Directive	Equipment Directive 97/23/EC. Only 0.77 m^2, 1.1 m^2 and 1.4 m^2 filters carry the CE mark.		

* Pilot and process scale only.

Conductivity / TOC



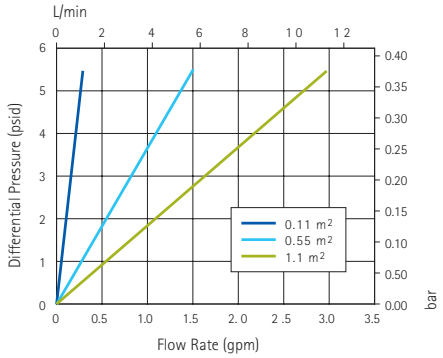
Conductivity Flush-up
Flow Rate 10 L/min



TOC Flush-up
Flow Rate 10 L/min

Water Permeability

Grade A1HC Pod Filters Example Graph



Water Flow Rates

Millistak+® CE Series

Media Type/Grade	Water Flow Rate L/min/m² at 10 psid, 23° C
CE15	3054.9 - 5611.5
CE20	2082.6 - 3825.5
CE25	1425.8 - 2619.1
CE30	974.1 - 1789.3
CE35	665.5 - 1222.4
CE40	454.6 - 835.1
CE45	310.6 - 570.5
CE50	212.2 - 389.8

Millistak+® HC Series

Media Type/Grade		Water Flow Rate L/min/m² at 10 psid, 23° C
A1HC	DE60	99.0 - 181.9
	DE75	31.6 - 58.0
B1HC	DE50	212.2 - 389.8
	DE75	31.6 - 58.0
C0HC	DE30	974.1 - 1789.3
	DE60	99.0 - 181.9
D0HC	CE25	1425.8 - 2619.1
	DE40	454.6 - 835.1
F0HC	DE60	99.0 - 181.9
	IM75	39.1 - 54.6
X0HC	IM75	39.1 - 54.6
	IM83	21.2 - 27.7

Millistak+® DE Series

Media Type/Grade	Water Flow Rate L/min/m² at 10 psid, 23° C
DE25	1425.8 - 2619.1
DE30	974.1 - 1789.3
DE35	665.5 - 1222.4
DE40	454.6 - 835.1
DE45	310.6 - 570.5
DE50	212.2 - 389.8
DE55	145.0 - 266.3
DE60	99.0 - 181.9
DE65	67.7 - 124.3
DE70	46.2 - 84.9
DE75	31.6 - 58.0

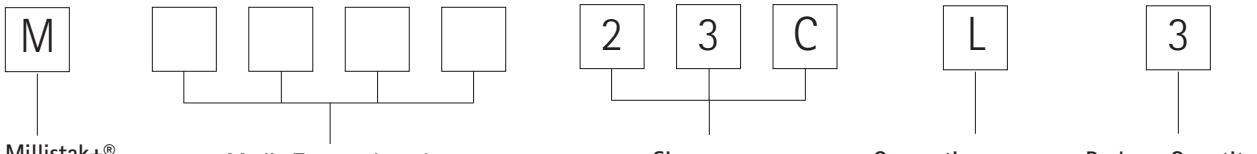
Choose the Right Media

Media Grade	Application	Characteristics	Media Construction
Single-layer CE*		Cellulose	CE15 to 50
Single-layer DE*		Cellulose + inorganic filter aid	DE 25 to 75
Triple-layer A1HC	Post-TFF (Prostak™ system) clarification fluids	Tightest media combination with an additional membrane layer to protect downstream membrane filters	DE60 + DE75 + RW01
Triple-layer B1HC	Post-centrifuge or settled permeate containing cellular particulate	A more open first layer withan additional membrane layer to protect downstream membrane filters	DE50 + DE75 + RW01
Double-layer C0HC	Perfusion bioreactor fluid	Two layers of a more open DE media	DE30 + DE60
Double-layer D0HC	Primary clarification directly out of the bioreactor	A more open CE layer and DE media combination	CE25 + DE40
Double-layer X0HC	Secondary clarification of bioreactor harvests, primarily for cell cultures	Two DE layers. Provides sterile filter protection without an RW01 membrane	IM75 + IM83
Double-layer F0HC	Secondary clarification of pretreated harvest by acid precipitation or flocculation, E. coli and yeast	Two DE layers. Provides sterile filter protection without an RW01 membrane	DE60 + IM75

*For clarification of serum, plasma, vaccines, cell culture or other fluids, choice of media grade should be based on small-scale trials.

Ordering Information

µPod® Filter



Millistak+®

Media Type and grade

A1HC	CE15	CE45	DE45
B1HC	CE20	CE50	DE50
C0HC	CE25	DE25	DE55
D0HC	CE30	DE30	DE60
F0HC	CE35	DE35	DE65
X0HC	CE40	DE40	DE70
			DE75

Size
23C = 23 cm^2

Connection
L = Luer Fitting

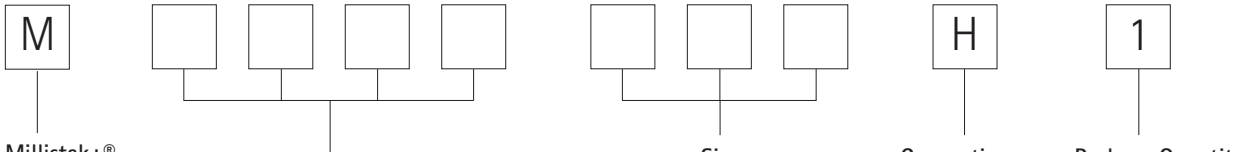
Package Quantity
3 = 3/pack

µPod® Filter Accessories

µPod® Tubing Kit Catalogue No. MTUBEKITL1

Gauge 0 - 60 psi and Connection Fittings Catalogue No. XXPXLGAGE

Lab Scale Pod Filter



Millistak+®

Media Type and grade

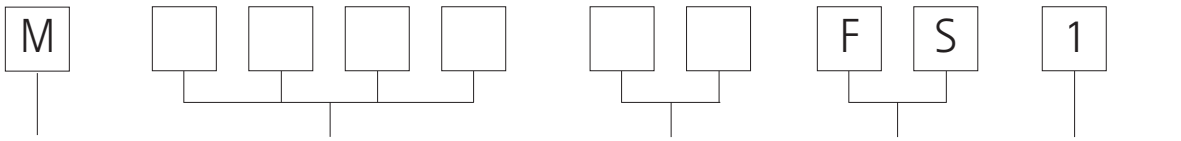
A1HC	X0HC	CE35	DE25	DE45	DE65
B1HC	CE15	CE40	DE30	DE50	DE70
C0HC	CE20	CE45	DE35	DE55	DE75
D0HC	CE25	CE50	DE40	DE60	
F0HC	CE30				

Size
027 = 0.027 m^2
054 = 0.054 m^2

Connection
H = $^1/_4$ in. (6 mm) Hose Barb

Package Quantity
1 = 1/pack

Multi Layer Process Scale Pod Filter



Millistak+®

Media Type and grade

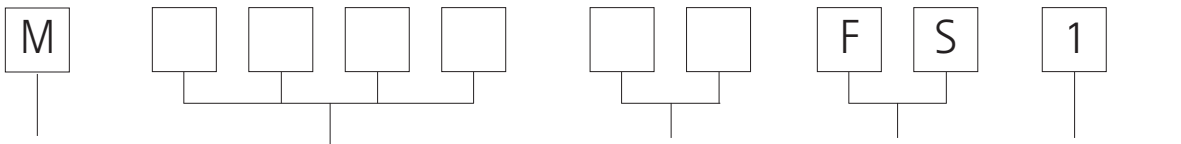
A1HC	C0HC	X0HC
B1HC	D0HC	F0HC

Size
01 = 0.11 m^2
05 = 0.55 m^2
10 = 1.1 m^2

Connection
FS = Flat seal

Package Quantity
1 = 1/pack

Single Layer Process Scale Pod Filter



Millistak+®

Media Type and grade

CE15	CE35	DE25	DE45	DE65
CE20	CE40	DE30	DE50	DE70
CE25	CE45	DE35	DE55	DE75
CE30	CE50	DE40	DE60	

Size
01 = 0.11 m^2
07 = 0.77 m^2
13 = 1.4 m^2

Connection
FS = Flat seal

Package Quantity
1 = 1/pack

Pilot and Process scale pods require a pod holder. Lab scale pods and µPod® filters do not require a holder.
Please contact your local sales representative for more information.

To place an order or receive technical assistance

In the U.S. and Canada, call toll-free
1(800)-645-5476

For other countries across Europe, call
+44 (0) 115 943 0840

For other countries across Europe and the world, please visit **www.emdmillipore.com/offices**

For Technical Service, please visit
www.emdmillipore.com/techservice

www.emdmillipore.com/millistak

Data Sheet

Hardware for Pod disposable depth filter systems

Innovative, high-performance Pods are ideal for primary and secondary clarification in lab, pilot and process-scale applications.

Millistak+® and Clarisolve® depth filter media are offered in a scalable, disposable format, the Pod Filter System. Accommodating applications from lab to pilot to process scale, the Pod format offers greater flexibility because of its unique modular design.

The Pod system is ideal for a wide variety of primary and secondary clarification applications, including cell cultures, yeast and *E. coli* lysates post centrifuge, *E. coli* refolds, media, vaccines, plasma proteins and sera.

The system's modular design allows users to operate the system with as few as one at pilot scale and as many as 30 Pod filters installed at the process scale. These options make it easy to configure a system for a specific application, and conveniently reconfigure it as process capacity requirements scale-up or down.

Benefits

- Modular format offers scalability from 5 to 12,000 liters or more
- Optional 100% disposable flow path eliminates need for housing, CIP, cleaning validation
- Robust construction is easy to use and set up
- Increase your installed surface area by 6x within the same footprint

EMD Millipore is a division of Merck KGaA, Darmstadt, Germany.

Linear Scalability

The innovative Pod filter system consists of seven filter sizes and two expandable holders. No matter what size Pod filter you choose, the same flow path and configuration ensures a linearly scalable solution from bench to process scale.

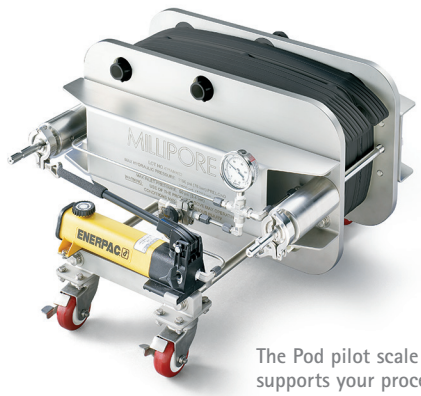
Easy to Use

With the compact, modular design of our Pod system, you can increase productivity and shorten cycle times.

Installation and set-up of the Pod system is simple and straightforward. The unique design of the disposable adapters makes it easy to connect the Pods to the process piping. The self-contained and disposable nature of the system protects operators from exposure to biohazards and eliminates maintenance as well as cleaning validation requirements.

Configurations

- **Pilot scale holder** – accommodates up to two full size Pods. An optional accessory kit expands capacity to 5 full scale Pods. Total surface area is dependent on media grade.
- **Process scale holder** – accepts from five to ten Pods per rack. Up to three racks can be stacked for process flexibility. Total surface area is dependent on media grade.
- **Disposable adapters** – connect Pods to process piping, creating disposable flow path.
- **Disposable diverter plates** – enable more than one media grade on a single rack
- **Disposable feed and filtrate manifolds** – make your flow path 100% disposable by replacing the stainless steel manifolds with disposable versions. Available for 1, 2, and 3 rack process scale holders.



The Pod pilot scale holder supports your process as you scale up.

Pod Holder Specifications*

Surface Area	Pilot Scale	Process Scale
Materials of construction Manifold Diverter plate End plates	 N/A Polypropylene 304 stainless steel	 316 L stainless steel Polypropylene 304 stainless steel
All metal surfaces in contact with process fluids	N/A	316 L stainless steel
Manifold surface finish, internal	N/A	Electropolished, Ra <0.5 µm (<20 micro-inches)
End plate clamp and guide rods	17–4 PH steel	17–4 PH steel
All other metal surfaces	304 stainless steel	304 stainless steel
TC gaskets	Thermoplastic Elastomer (TPE)	Thermoplastic Elastomer (TPE)
TC clamp	304 stainless steel 2 piece clamp	304 stainless steel 2-piece clamp
Performance properties	Capable of supporting and sealing pod filters up to 50 psig maximum operating pressure at 25 °C. Inlet and outlet connection to the pods and vents are via disposable adapters.	
Maximum differential pressure Forward Reverse	 50 psid (3.5 bar) at 25 °C; 15 psid (1.0 bar) at 80 °C 30 psid (2.1 bar) at 25 °C	
Regulatory information	Sealing materials and plastics in contact with the product meet USP <88> biological reactivity test for Class VI plastics and are Title 21 CFR 177.2600 and 177.1550 compliant.	

Pod Disposable Manifold Specifications*

Pod Disposable Manifold	Specifications
Materials of construction Polypropylene Double braided silicon tubing Silicone gaskets Glass filled nylon clamps	Max. operating pressure: 50 psi Hot water sanitization: 1 cycle of 80 °C for 30 minutes Toxicity: Component materials comply with the requirements of USP <88> biological reactivity tests for Class IV plastics

*No holder required for lab scale pod

Ordering Information

Description	Qty/Pk	Catalogue No.
Pilot Scale Holder		
For pod configurations from 1 to 2 filters	1	MP0DPILOT
Pilot holder expansion kit allows for pod configurations up to 5 filters	1	MP0DPILOTX
Process Scale Holders		
1-rack holder; for 5 to 10 filters; Gemü® valves	1	MP0DSYS1A
1-rack holder; for 5 to 10 filters; ITT valves	1	MP0DSYS1B
1-rack holder; for 5 to 10 filters; no valves	1	MP0DSYS1N
1-rack expansion kit; for 5 to 10 filters; no valves or casters	1	MP0DSYS1X
2-rack holder; for 5 to 20 filters; Gemü® valves	1	MP0DSYS2A
2-rack holder; for 5 to 20 filters; ITT valves	1	MP0DSYS2B
3-rack holder; for 5 to 30 filters; Gemü® valves	1	MP0DSYS3A
3-rack holder; for 5 to 30 filters; ITT valves	1	MP0DSYS3B
Holder Replacement Parts*		
Hydraulic pump		MP0DHYPUMP
Hydraulic system pressure gauge		MP0DHYGAGE
Hydraulic fluid		MP0DHFLUID
Clamp insert		MP0DINSERT
1.5 in. TC stainless steel clamp for use with MP0DINSERT		YY2004045
Clamp rod knob		MP0DCRKN0B
Clamp rod for 2 filters		MP0DCR0D02
Clamp rod for 5 filters		MP0DCR0D05
Clamp rod for 10 filters		MP0DCR0D10
Manifold elbow, 90 °C, 1.5 in. 316 stainless steel		MP0DSSELB0
Manifold tee, 1.5 in. 316 stainless steel		MP0DSSTEE
Manifold spool, 1 in. x 6.60 in. L		MP0DMANSPH
Manifold spool, 1.5 in. x 13.16 in. L		MP0DMANSPV
Manifold bracket assembly		MP0DMANBRK
Replacement diaphragm for 1 in. Gemü® MP0DVALVEA		MP0DVLVADIA
Replacement diaphragm for 1 in. ITT MP0DVALVEB		MP0DVLVBDIA
Holder Accessories*		
1-rack Disposable feed and filtrate manifold		MP0DDSPMAN1
2-rack Disposable feed and filtrate manifold		MP0DDSPMAN2
3-rack Disposable feed and filtrate manifold		MP0DDSPMAN3
Disposable adapter kit** 3 through adapters, 3 blind adapters	1	MP0DADAPT
Disposable adapter kit** 6 through adapters, required if using MP0DDIVERTR	1	MP0DADPTF
1.5 in. TC sanitary gauge, 0–4 bar (0–60 psi)	1	MP0D60PSIG
1.5 in. TC EPDM gasket	10	HGTC150EP
1.5 in. TC stainless steel clamp	1	YY2004045
Diaphragm valve, 1 in. Gemü®	1	MP0DVALVEA
Diaphragm valve, 1 in. ITT	1	MP0DVALVEB
Disposable diverter plate	10	MP0DDIVERTR
Pod pilot holder handle	1	MP0DPLTHNDL
End Plate Replacement Kit This kit replaces the bronze bushings with linear ball bearings to facilitate movement of the end plate. The kits come with one end plate, new guide rods and associated hardware.		
Pod Retrofit Kit for MP0DPILOT		MP0DRET1
Pod Retrofit Kit for MP0DPILOT with extension rods		MP0DRET2
Pod Retrofit Kit for process scale holders		MP0DRET3

*Consult your sales associate for replacement part and accessory availability.

**The disposable adapter kit must be ordered with individual Pod filters in order to install the Pod filter in the holder.

To Place an Order or Receive Technical Assistance

In the U.S. and Canada, call toll-free
1(800)-645-5476

For other countries across Europe, call
+44 (0) 115 943 0840

For other countries across Europe and the world, please visit **www.emdmillipore.com/offices**

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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.

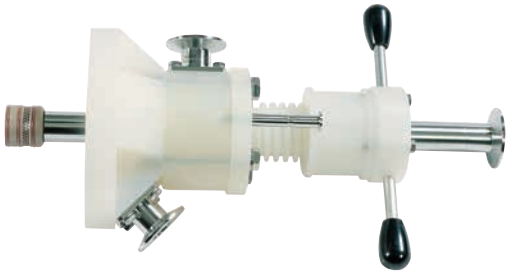


Fig 2. The Chromaflow nozzle that enables packing in place in a fully assembled column (GE Healthcare patent).

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

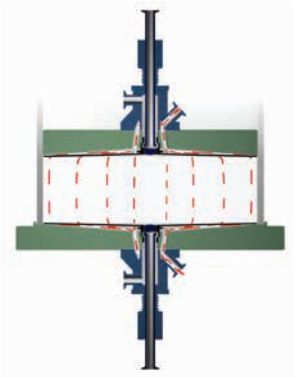
Improved safety is another advantage of the Chromaflow column concept. Because all the column operations are performed in a "closed system" environment, there is less risk of the operator coming into contact with hazardous chemicals and of the target product being exposed to contamination. In this way, overall safety and hygienic operation are improved.

Principle of operation

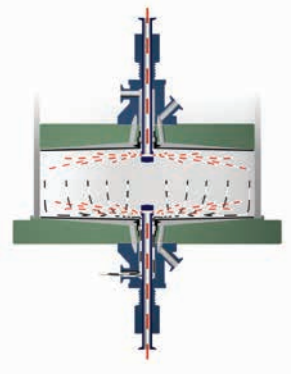
The column has a three-position nozzle located in the center of the top and bottom bed support. These three positions enable packing, unpacking, operation and cleaning to be performed without any adjustments to the assembled column, that is the lid remains in place.

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 to 300 mm, 200 to 400 mm and 300 to 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 × mm)
Chromaflow column 400/100-300*	3	12.6–37.8	1568	230	700 × 700
Chromaflow column 600/100-300	3	28.3–84.9	1568	375	800 × 800
Chromaflow column 800/100-300	3	50.3–150.9	1572	610	1000 × 1000
Chromaflow column 1000/100-300	3	78.5–235.5	1573	930	1200 × 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 316	No

EPDM = ethylene propylene diene, FEP = fluoroethenepropene, 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 × H × 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
Sepharose™ Fast Flow media	500	11	250	5.5	500	24	250	12	500	42	250	21	500	66	250	33
Sepharose 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

Chromaflow columns with acrylic tubes	Bed support 10 mm SS sinter	Bed support 20 mm SS sinter	Bed support 20 mm PE sinter
I.d. 400 mm Man. nozzle			
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.d. 400 mm Auto. nozzle			
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.d. 400 mm SFP Man. nozzle*			
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.d. 400 mm SFP Auto. nozzle			
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.d. 600 mm Man. nozzle			
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.d. 600 mm Auto. nozzle			
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.d. 800 mm Man. nozzle			
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.d. 800 mm Auto. nozzle			
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.d. 1000 mm Man. nozzle			
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.d. 1000 mm Auto. nozzle			
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 number
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 number
Valves	
4 port 2 way, i.d. 10 mm, 25 mm TC	18-1012-56
4 port 4 way, i.d. 10 mm, 25 mm TC	18-1012-57
3 port 2 way, i.d. 15 mm, 25 mm TC	44-5499-90
4 port 4 way, i.d. 20 mm, 51 mm TC	44-2302-01
3 port 2 way, i.d. 22 mm, 51 mm TC	44-1583-01
3 port 2 way, i.d. 35 mm, 51 mm TC	44-5494-65
Valve sealing washer Fits 10 mm 2- and 4-way valves	18-1128-69
PVC tubing with sanitary fitting 25 mm TC	
i.d. 10 mm, 900 mm	18-1012-62
i.d. 10 mm, 1400 mm	18-1012-63
i.d. 10 mm, 1700 mm	18-1012-64
i.d. 10 mm, 2000 mm	18-1012-87
i.d. 14 mm, 750 mm	18-1027-28
i.d. 14 mm, 1800 mm	18-1027-29
PVC tubing with sanitary fitting 51 mm TC	
i.d. 22 mm, 900 mm	44-1616-09
i.d. 22 mm, 1400 mm	44-1616-08
i.d. 22 mm, 2000 mm	44-1616-07
i.d. 22 mm, 4000 mm	44-1616-06
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, 2×25 mm TC, 1×51 mm TC	18-1003-63
Castors, assembly kit 400-600	18-1171-51
Castors, assembly kit 800-1000 The kit contains a complete set of wheels, fasteners and adapters for a column.	18-1171-52
Pressure sensor i.d. 10 mm, 25 mm TC	44-0507-02
Pressure sensor i.d. 22 mm, 51 mm TC	44-0507-03

Designation	Code number
Media stirrers	
Media stirrer, 80 cm	18-1149-80
Media stirrer, 150 cm	18-1149-81
Connectors	
i.d. 10, 25 mm TC-3/4″-20 UNF threaded	18-1012-68
i.d. 10, 25 mm TC-i.d. 14, 51 mm TC	18-1027-25
i.d. 14, 51 mm TC-i.d. 22, 51 mm TC	18-1027-26
Chromaflow Nozzle control unit	18-1164-61
Chromaflow Nozzle pipings	
Chromaflow Nozzle piping 400 1/2”	18-1172-01
Chromaflow Nozzle piping 400 3/4”	18-1172-00
Chromaflow Nozzle piping 400 1”	18-1171-99
Chromaflow Nozzle piping 600 1/2”	18-1172-06
Chromaflow Nozzle piping 600 3/4”	18-1172-05
Chromaflow Nozzle piping 600 1”	18-1172-04
Chromaflow Nozzle piping 800 1/2”	18-1171-94
Chromaflow Nozzle piping 800 3/4”	18-1171-93
Chromaflow Nozzle piping 800 1”	18-1171-92
Chromaflow Nozzle piping 1000 1/2”	18-1172-09
Chromaflow Nozzle piping 1000 3/4”	18-1172-08
Chromaflow Nozzle piping 1000 1”	18-1172-07

For local office contact information, visit
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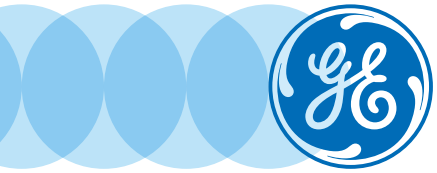

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18-1138-92 AF 10/2014

MabSelect SuRe™ LX

MabSelect SuRe LX is an alkali-stabilized, protein A-derived affinity medium with a binding capacity for monoclonal antibodies (MAbs) exceeding that of MabSelect SuRe at longer residence times. As an example, at 6 min residence time, the dynamic binding capacity of MabSelect SuRe LX for human IgG is approximately 60 g/l. This special combination of high binding capacity plus alkaline stability gives manufacturers of MAbs many opportunities to improve process economics and product quality.

High dynamic binding capacity (DBC) helps users process feed from high-expression cell cultures with increased antibody titers in shorter time or with smaller chromatography unit operations. Enhanced alkaline stability means that regular cleaning-in-place (CIP) can be performed with cost-effective agents such as sodium hydroxide (NaOH) to prolong the medium's working lifetime.

Key performance benefits of MabSelect SuRe LX include:

- Outstanding binding capacity, for example, approx. 60 g/l medium for human IgG at 6 min residence time
- Quick, efficient processing of large volumes of high-titer bioreactor feeds
- Higher density eluates increase operating flexibility and allow smaller unit operations
- Effective CIP with 0.1 M NaOH over hundreds of purification cycles improves process economy
- Enhanced protease resistance of the protein A ligand reduces leakage
- Generic elution conditions for different MAbs enable platform purifications

Fig 1. The significantly higher binding capacity of MabSelect SuRe LX protein A-based affinity media allows MAb manufacturers to process high-titer feeds in relatively small production columns.

Medium characteristics

Well-established in bioprocessing

The MabSelect™ media family for the process-scale capture and purification of MAbs comprises MabSelect, MabSelect Xtra™, MabSelect SuRe, and MabSelect SuRe LX.

MabSelect SuRe LX has been further developed from MabSelect SuRe to give even higher binding capacity at longer residence time. Table 1 lists the main characteristics of MabSelect SuRe LX.

Table 1. Main characteristics of MabSelect SuRe LX

Matrix	Rigid, highly cross-linked agarose
Ligand	Alkali-stabilized, protein A-derived (*E. coli*)
Ligand coupling	Single-point attachment
Coupling chemistry	Epoxy
Average particle size (d_{50v})*	85 µm
Dynamic binding capacity†	Approx 60 mg human IgG/ml medium at 6 min residence time
Maximum mobile phase velocity‡	500 cm/h
pH working range	3–12
Chemical stability	Stable in all aqueous buffers commonly used in protein A chromatography
Cleaning-in-place stability	0.1–0.5 M NaOH
Delivery conditions	20% ethanol

* d_{50v} is the median particle size of the cumulative volume distribution.

† Determined at 10% breakthrough by frontal analysis at a mobile phase velocity of 100 cm/h in a column with a bed height of 10 cm, residence time is 6 min. Residence time is equal to bed height (cm) divided by nominal fluid velocity (cm/h) during sample loading. Nominal fluid velocity is equal to volumetric flow rate (ml/h) divided by column cross-sectional area (cm^2).

‡ Determined in an AxiChrom™ 300 column, bed height 20 cm, operating pressure less than 2 bar.

High binding capacity meets modern processing demands

Increasing demand for MAbs as biopharmaceuticals has promoted the development of cell cultures with increased expression levels. Over recent years, the antibody titers of mammalian cell cultures have risen dramatically. Titers of 5 to 10 g/l are not unusual today. If MAb purification processes are to handle high-titer bioreactor feeds quickly and cost-effectively, they must offer significant increases in dynamic binding capacity (DBC). Several studies show that this can be achieved by increasing residence time with MabSelect SuRe LX (Fig 2).

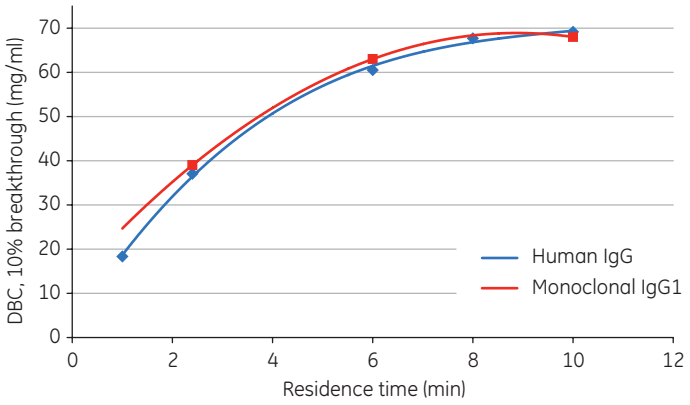

Fig 2. Dynamic binding capacity increases as a function of residence time.

Moreover, direct comparisons between MabSelect SuRe LX and MabSelect SuRe, which already exhibits a high DBC, show that the former offers more than 20% higher DBC at extended residence times. At 6 min, for example, the DBC of MabSelect SuRe LX at 10% breakthrough for seven MAbs is clearly superior to that of MabSelect SuRe (Fig 3). These data confirm that the increased capacities range from approximately 20% to 50%.

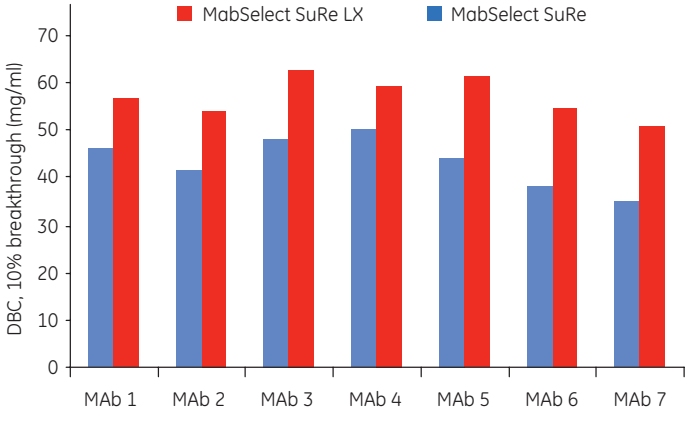

Fig 3. Significantly increased DBC of MabSelect SuRe LX compared to MabSelect SuRe at a residence time of 6 min.

This high capacity also translates to smaller elution pool volumes, that is, higher antibody concentrations (large pool volumes are a common bottlekneck in many manufacturing facilities today). Note that the high rigidity of the medium (see below) permits the use of higher bed heights, which increases the flexibility of process design and large-scale operations.

High alkaline stability extends working lifetime

CIP with NaOH is a key step in the cost-effective production of pure MAb products at industrial scale. However, affinity media based on native or recombinant protein A (rProtein A) ligands are particularly sensitive to NaOH and this is generally regarded as a drawback of the method. MabSelect SuRe LX overcomes this limitation by using the same alkali-stablilized ligand as MabSelect SuRe. The ligand was developed by protein engineering one of the IgG-binding domains of protein A. Amino acids particularly sensitive to alkali were identified and substituted with more stable ones. The final construct is a tetramer of the engineered domain with a C-terminal cysteine, which enables single-point attachment to the matrix. The resulting highly pure ligand is immobilized to the agarose matrix via a chemically stable thio-ether linkage.

The increased alkaline stability allows very effective CIP with 0.1 to 0.5 M NaOH over many purification cycles (Figs 8 and 9). In addition, the ligand shows improved stability to proteases compared with rProtein A. This attribute also extends working lifetime and minimizes ligand leakage. Furthermore, as the engineered protein A ligand of MabSelect SuRe LX does not exhibit affinity for the Fab region of antibodies, more generic elution conditions can be employed compared with rProtein A. Antibodies can thus be eluted at a more homogeneous pH range (1). See Figure 7 for more details.

Rigid, highly cross-linked matrix allows high flow rates

Like other media in the MabSelect family, MabSelect SuRe LX features a rigid, highly cross-linked agarose base matrix that allows much higher flow rates in process-scale purification than conventional cross-linked agaroses of similar porosity. This permits high-throughput purification of MAbs from large volumes of feed. Figure 4 shows pressure/flow curves for MabSelect SuRe LX packed in a range of column sizes.

High rigidity allows column capacity to be increased for high-titer feeds by increasing the column bed height. Running at higher bed heights and flow rates gives greater flexibility when designing processes, and can reduce the need to purchase new hardware. Higher bed heights also mean small diameter columns and thus a reduced equipment footprint.

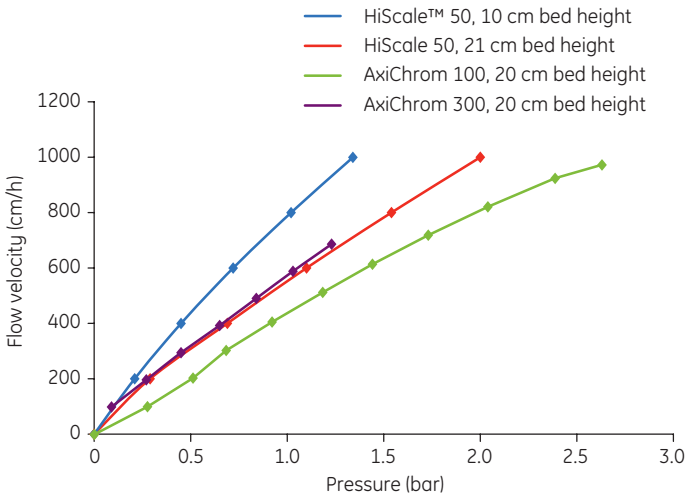

Fig 4. Pressure/flow curves for MabSelect SuRe LX packed at different bed heights in HiScale 50 and AxiChrom 100 and 300 columns. The medium's rigid base matrix allows high flow rates in process-scale purifications.

BioProcess™ medium with full support

MabSelect SuRe LX also belongs to the BioProcess media family that is developed and supported for the large-scale manufacture of biopharmaceuticals. This support includes validated manufacturing methods, secure long-term media supply, safe and easy handling, and Regulatory Support Files (RSF) to assist process validation and submissions to regulatory authorities. In addition, Fast Trak Training & Education provide high-level, hands-on training for all key aspects of bioprocess development and manufacturing.

Operation

Equipment

MabSelect SuRe LX can be used with most modern chromatography equipment from laboratory to production scale. Table 2 lists suitable empty columns from GE Healthcare. To ensure best performance at process scale, pack MabSelect SuRe LX at bed heights of 10 to 30 cm.

Table 2. Recommended GE Healthcare column families for packing MabSelect SuRe LX

Column family range		Inner diameter (mm)
Laboratory scale:	HiScale	16, 26, and 50
Pilot and production scale:	AxiChrom*	50–1000
	BPG™	100–300†
	Chromaflow™‡	400–800§

* Intelligent Packing method for MabSelect SuRe can be used.

† The pressure rating of BPG 450 is too low for use with MabSelect media.

‡ Packing instructions for MabSelect media in Chromaflow columns are described in Application note 11-0007-52.

§ Larger pack stations can be required for larger diameters.

Method development and scale-up

The primary aim of method development is to establish and optimize the conditions that will bind the highest amount of target molecule in the shortest time, and with the highest product recovery.

The degree to which IgG binds to protein A varies with respect to both origin and antibody subclass. In general, however, human or humanized antibodies, except for subclass 3, have high affinity for protein A.

MabSelect SuRe LX is supplied prefilled in 96-well Predictor™ plates, which support high-throughput process development (HTPD) by allowing parallel screening of chromatographic conditions such as pH and conductivity.

Defined conditions for loading, washing, elution, CIP, etc., can then be verified and optimized with small prepacked HiScreen™ (4.7 ml) columns. Together with a chromatography system such as ÄKTA™ avant, the HiScreen format helps develop an efficient and robust separation method.

Further development and optimization using HiScale columns then permits straightforward scale-up for GMP clinical trials or full-scale manufacturing on AxiChrom columns.

Loading and elution

The high selectivity of MabSelect SuRe LX renders efficiency-related parameters such as sample load, flow rate, bead size, and bed height less important for resolution. The primary aim of method optimization is, therefore, to establish the conditions that will bind the highest amount of target molecule and give the highest product recovery.

Typically, clarified feedstock is loaded directly onto the column. The amount of antibody that can be loaded is determined by the dynamic binding capacity (DBC). Since DBC increases as a function of residence time and varies between different MAbs and starting materials, we recommend determining DBC at different residence times (Fig 2). To obtain high and reproducible yields over hundreds of cycles, the load should normally not exceed 90% of DBC.

After intermediate washing, the target MAb is normally eluted at pH 3 to 4. Elution conditions for a specific MAb can be determined by performing elution in a linear pH gradient. Figure 5 shows an example run for MabSelect SuRe. Elution pH was 3.67 at peak maximum and 3.56 at 10% peak maximum (i.e. descending). Based on this result, an elution pH of 3.5 would result in high yields and narrow elution peaks.

Running conditions

Column: HiScreen MabSelect SuRe, 4.7 ml
Sample: 1 ml of clarified CHO feed containing 1.72 mg MAb/ml
Binding buffer: 20 mM citrate, pH 6.0
Elution buffer: 20 mM citrate, pH 3.0
Gradient: Linear, 20 mM citrate buffer pH 6.0 to 3.0 in 10 CV
Flow rate: 0.5 ml/min
System: ÄKTA avant 25

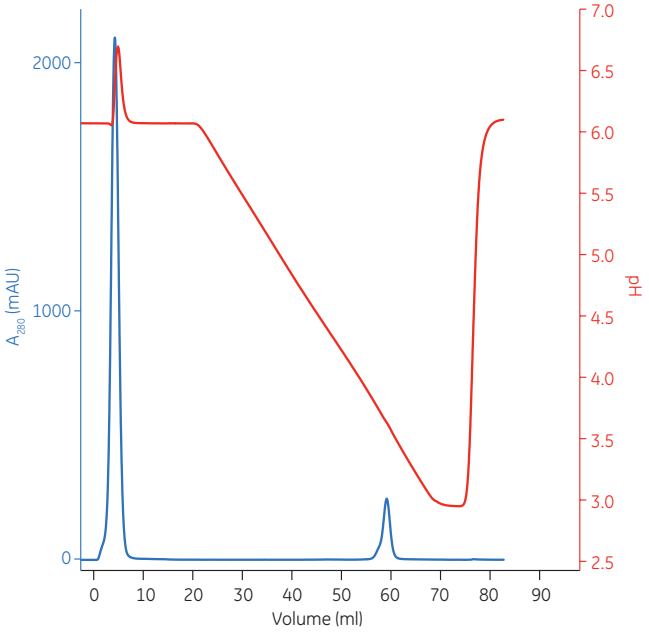

Fig 5. Determining optimum elution pH helps ensure a high yield of the MAb product.

Design of Experiments (DoE) can also be used to optimize elution conditions. In the DoE example shown in Figure 6, elution pH was varied between 3.25 to 4.0 and flow rate between 0.3 and 1 ml/min (100 to 300 cm/h). Highest yields and lowest pool volumes were obtained at low elution pH, while no major effect of flow rate could be observed. The optimal elution pH for the investigated MAb was 3.6 or below.

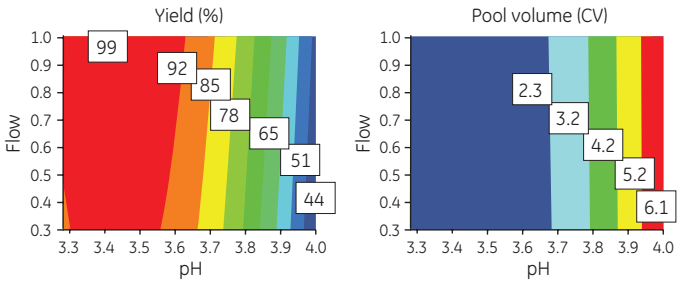

Fig 6. DoE optimization of elution conditions on MabSelect SuRe LX. CV=column volume.

Generic elution promotes platform purification

MabSelect SuRe LX allows the use of generic elution conditions for different monoclonal antibodies, which is advantageous when designing generic purification platform processes. Figure 7 shows the elution pH for different MAbs with both MabSelect (with a traditional rProtein A ligand) and with MabSelect SuRe. With MabSelect, the MAbs elute at different pHs, but for MabSelect SuRe, almost all elute at a more homogeneous pH. A similar behavior is expected for MabSelect SuRe LX.

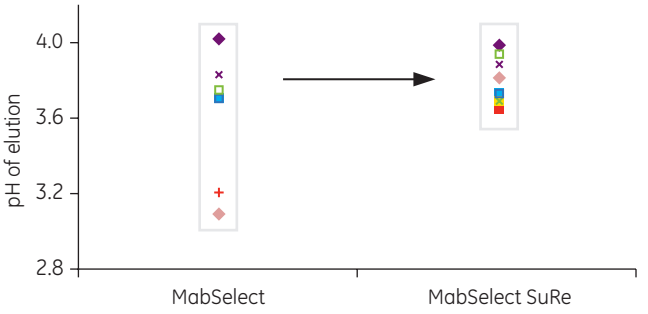

Fig 7. Scatter plot showing the distribution of elution, pH of various human antibodies and Fc fusion proteins on MabSelect and MabSelect SuRe. Reprint from *Biotechnol. Bioeng.* (1), with courtesy of Amgen.

Effective CIP with retained dynamic binding capacity

Use of 0.1 to 0.5 M NaOH is recommended for CIP and sanitization. As well as being an effective cleaning agent, NaOH is also inexpensive and easy to handle in bulk quantities. It is thus an attractive choice for large-scale commercial manufacturers of monoclonal therapeutic antibodies.

A lifetime study with MAb-containing feedstock has shown that the DBC and yield of MabSelect SuRe LX are stable over 100 purification cycles with 0.1 M NaOH, and that the levels of leached protein A and host cell proteins remain constant. Figure 8 shows DBC data and Figure 9 overlay chromatograms from this study.

Effective sanitization of MabSelect SuRe LX is also possible using a combination of 0.1 M NaOH and 40% isopropyl alcohol.

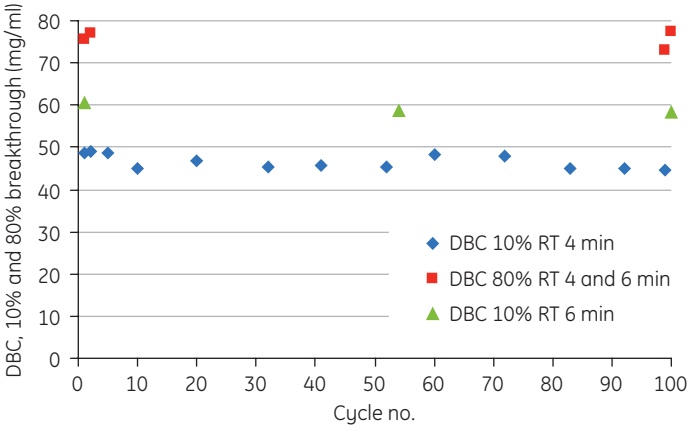

Fig 8. Dynamic binding capacity measurements for MabSelect SuRe LX over 100 purification cycles with 0.1 M NaOH as CIP agent. RT = residence time.

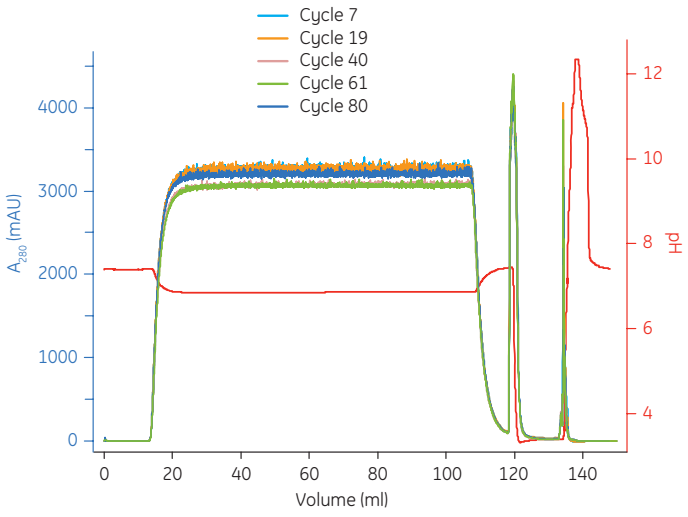

Fig 9. Overlay of chromatograms from runs with harvested cell culture feed (HCCF), (0.8 g MAb/l from cycle 3). A new batch of HCCF with a MAb concentration of 1.1 g/l was applied from cycle 87.

An extended lifetime study on human IgG with repeated buffer cycles also demonstrated that DBC is stable (> 95%) for more than 300 cycles with 0.1 M NaOH. For 0.5 M NaOH, DBC gradually decreases after cycle 25 but still remains above 90% for 100 cycles at this higher concentration.

Full details can be found in Application note: Lifetime performance study of MabSelect SuRe LX during repeated cleaning-in-place (see Related literature)

Storage

Store unused MabSelect SuRe LX in its container at a temperature of 2°C to 8°C. Ensure that the screw-top is fully tightened. Equilibrate packed columns in buffer containing 20% ethanol or 2% benzyl alcohol to prevent microbial growth.

After storage, equilibrate with starting buffer and perform a blank run, including CIP, before use.

Reference

1. Ghose G, *et al.* Antibody variable region interactions with protein A: Implications for the development of generic purification processes. *Biotechnol. Bioeng.* **92(6)** 665-673 (2005).

Ordering information

Product*	Quantity	Code no.
MabSelect SuRe LX	25 ml	17-5474-01
	200 ml	17-5474-02
	1 l	17-5474-03
	5 l	17-5474-04
	10 l	17-5474-05
PreDictor MabSelect SuRe LX, 6 µl	4 × 96-well plates	17-5474-30
PreDictor MabSelect SuRe LX, 20 µl	4 × 96-well plates	17-5474-31
PreDictor MabSelect SuRe LX, 50 µl	4 × 96-well plates	17-5474-32
HiScreen MabSelect SuRe LX	1 × 4.7 ml	17-5474-15

* MabSelect Sure LX will be made available in prepacked, prequalified, and presanitized ReadyToProcess™ columns. Please ask for details.

Related products

HiScale 16/20	1	28-9644-41
HiScale 16/40	1	28-9644-24
HiScale 26/20	1	28-9645-14
HiScale 26/40	1	28-9645-13
HiScale 50/20	1	28-9644-45
HiScale 50/40	1	28-9644-44

Related literature

Data files

MabSelect	18-1149-94
MabSelect Xtra	11-0011-57
MabSelect SuRe	11-0011-65

Application notes

Lifetime performance study of MabSelect SuRe LX during repeated cleaning-in-place	28-9872-96
Dynamic binding capacity study on MabSelect SuRe LX for capturing high-titer monoclonal antibodies	28-9875-25
High-throughput process development for design of cleaning-in-place protocols	28-9845-67

Handbooks

Antibody Purification, Principles and methods	18-1037-46
High-throughput Process Development with PreDictor Plates, Principles and methods	28-9403-58

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Shinjuku-ku, Tokyo 169-0073
Japan

28-9870-62 AA 02/2011

Data Sheet

Cogent® Process-Scale Tangential Flow Filtration System

A fully-automated, configurable, TFF system suited for manufacturing of biopharmaceuticals and cGMP process-scale applications

The fully automated Cogent® TFF system is designed to separate and purify monoclonal antibodies, vaccines, plasma, and therapeutic proteins. It is ideally suited for both pilot and production scale applications, thereby supporting rapid scale up from small to large scale operations.

Benefiting from our leading bioprocess knowledge and engineering expertise, the Cogent® Process Scale System is the culmination of 25 years of custom system design and incorporates many unique, innovative and intelligent design features. This system has a very low hold-up volume for maximum volume concentration and optimal product recovery, thus enhancing process performance.

Benefits:

- Modular standard options allow the unique system configuration that best matches process requirements while minimizingupfront investment.
- Full process automation eases the consistent production of preclinical and clinical scale quantities of high-value drug products to cGMP standard.
- Optimized design and component integration of NovAseptic® valves and TFF cassette holders result in a low minimum working volume and ensure maximum product recovery.
- Designed to maximize TFF performances in fed-batch, concentration, total recycle or single pass mode.
- Comprehensive services ensure rapid implementation and optimized performance.

EMD Millipore is a division of Merck KGaA, Darmstadt, Germany

Configure your system according to your process needs...

Option 1: Tank (50, 100, 200L)

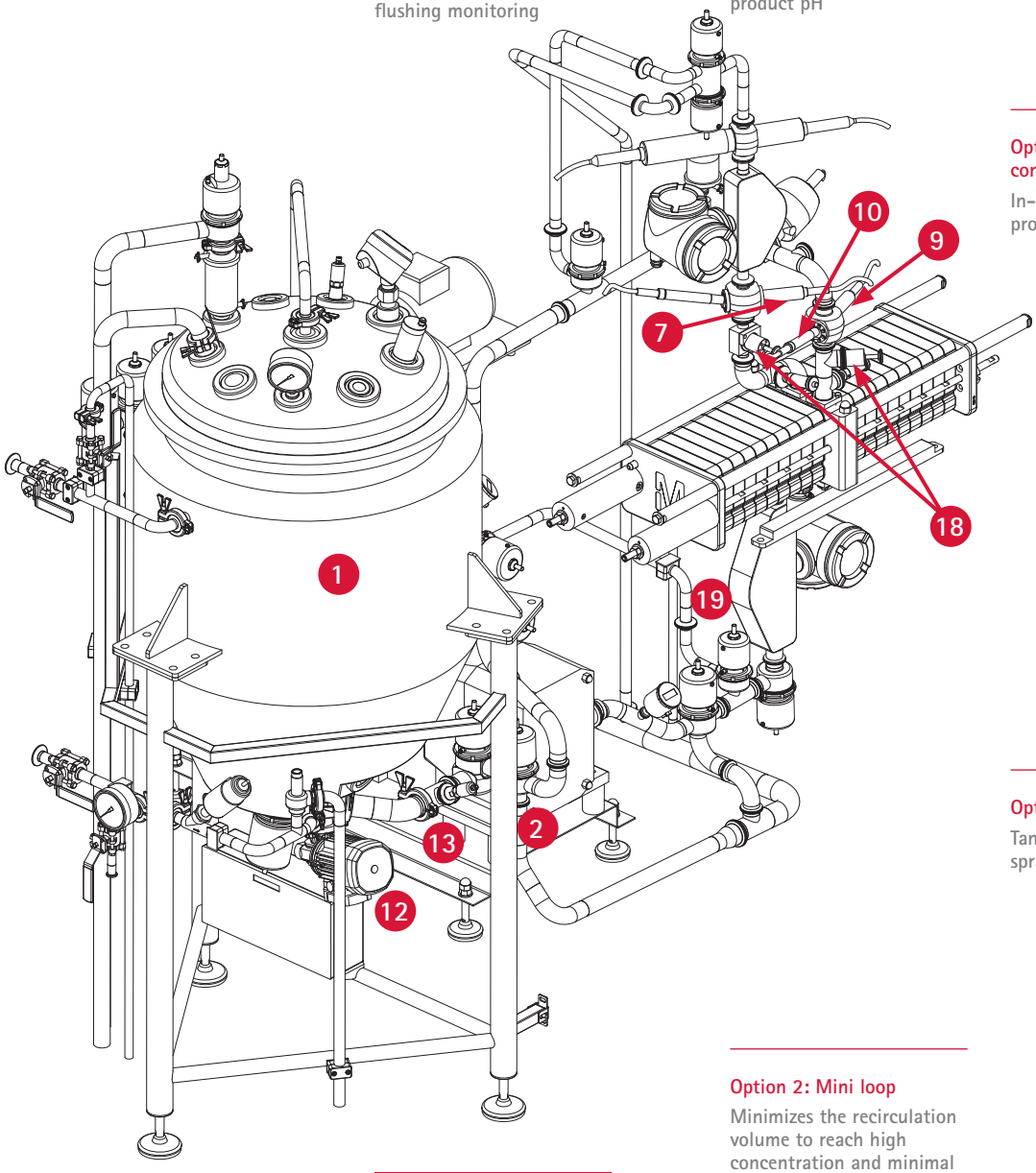
Jacketed for temperature regulation

Option 7: Filtrate conductivity

Measurement of a wide range of products (WFI, buffer solutions, protein solutions) or post CIP flushing monitoring

Option 10: Retentate pH

In-process monitoring of product pH



Option 9: Retentate conductivity

In-process monitoring of product conductivity

Option 18: Retentate and Filtrate NovaSeptum® Sampling port

In-process sterile sampling of product

Option 19: Spray ball valve

Tank cleaning using the spray ball

Option 2: Mini loop

Minimizes the recirculation volume to reach high concentration and minimal product volume

Option 12: Tank NovAseptic® GMP mixer

Ensures product homogeneity, specially important during diafiltration step. Aseptic design, minimized shearing

Option 13: Tank Outlet Level Switch

Allows to stop the feed pump when air reaches this sensor. E.g: In Mini loop concentration mode, detects the end of the step (tank fully empty).

Option 3: Transfer Pump

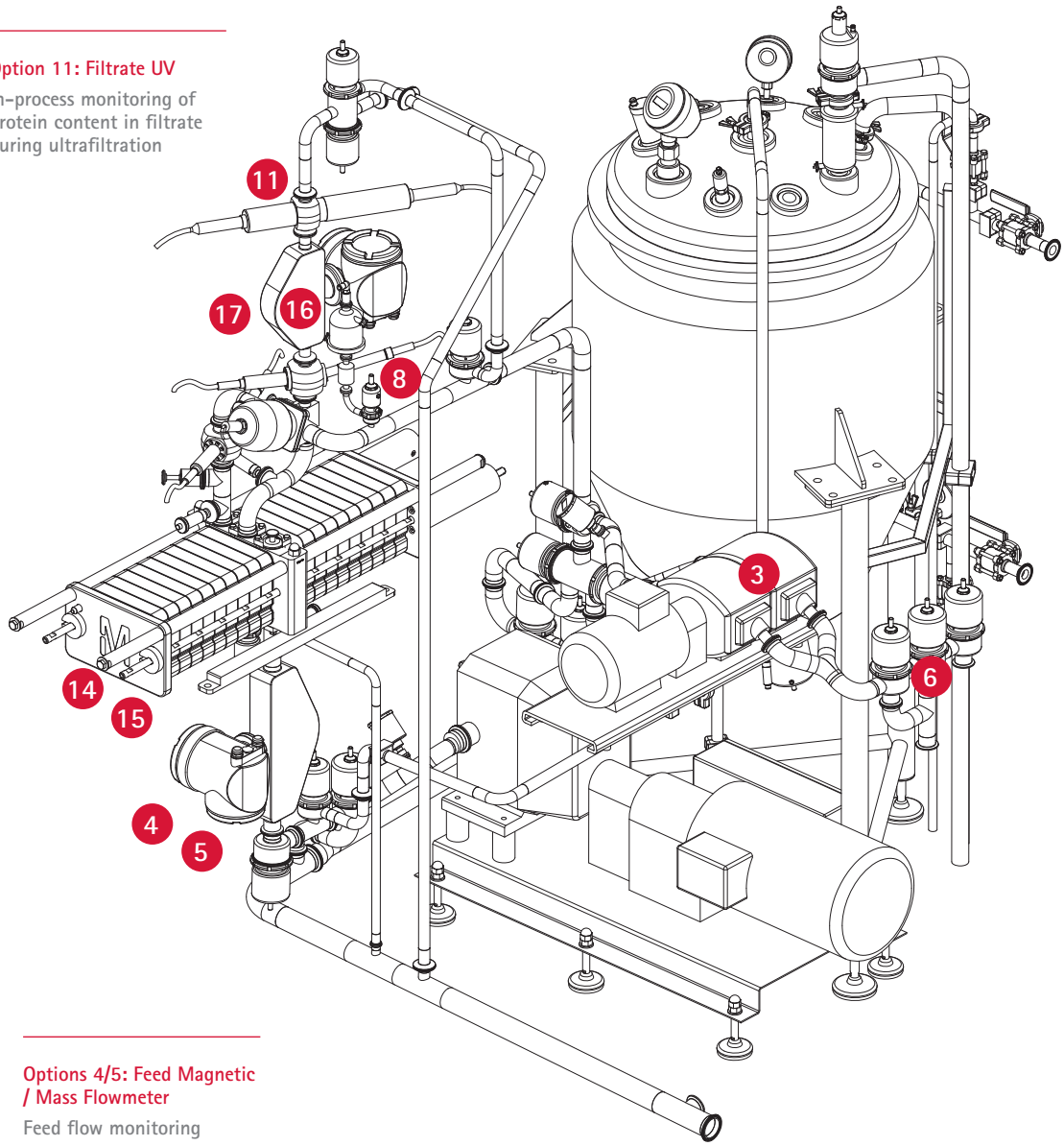
Transfer of product / buffers into the feed tank from any other tank. Allows fed-batch mode, and diafiltration.

Option 8: Filtrate pH

pH monitoring during cleaning and sanitization procedures

Option 11: Filtrate UV

In-process monitoring of protein content in filtrate during ultrafiltration



Options 16/17: Filtrate Mass / Magnetic flowmeter

Filtrate flow and total volume monitoring in diafiltration mode

Options 14/15: Process Scale Holder

Can be configured either with manual or hydraulic closure. Hydraulic closure can be done with a hand pump or with an automated hydraulic box.

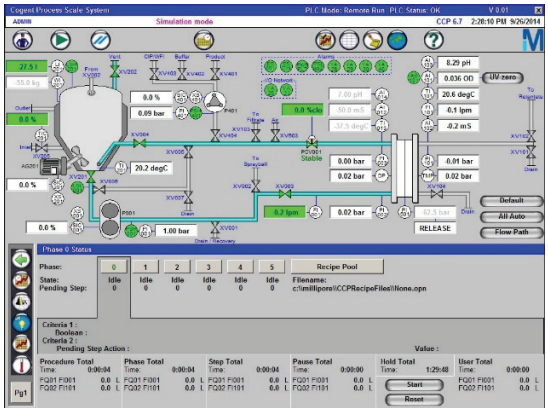
Options 4/5: Feed Magnetic / Mass Flowmeter

Feed flow monitoring

Option 6: Transfer Inlet Manifold

Allows connecting several inlets to the transfer pump head (product/WFI/CIP) at the same time, avoiding many connections / disconnections

...and build a consistent user experience



Total Process Control and Connectivity

The Cogent® Process Scale system is easily controlled via the Common Control Platform® (CCP®) software, a powerful, intuitive and graphical software that provides real-time monitoring and total in-depth control of your TFF process.

Using robust PCs, PLCs, and SCADA® technology, it meets the most stringent standards for connectivity, reliability and ease of use.

Benefits:

- Create process operations using the recipe editor, monitor or control the process in the home screen, and create reports for the batch using the configurable report generator
- Developed under GAMP guidelines and FDA 21 CFR Part 11 compliance-ready, including audit trails and electronic signatures for verification
- Sensor combinations can be adapted to process requirements allowing the maximum confidence in process monitoring
- Utilities to connect all of your separation unit operations to a central network or DCS (e.g. Delta V)
- Used on multiple unit operations CCP® software provides one familiar interface to simplify software management and reduce learning curves

NovAseptic® GMP mixer

Embedded NovAseptic® Valves, Mixer and Connectors

Engineered for optimal performance, reliability, durability and ease of maintenance.

The design and development of each component is based on more than 20 years' experience, focused on aseptic application. This is why we choose to call it "Aseptic by Design."

Benefits:

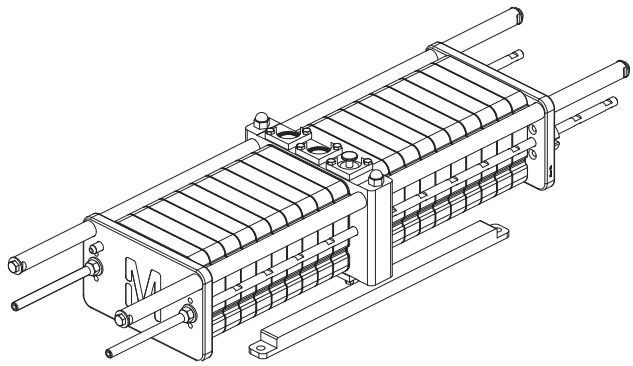
- Comply with cGMP Design Qualification criteria for aseptic processing
- NovAseptic® connector ensures no dead legs and maximum product recovery with zero hold up volume.
- Comply with the most stringent cleaning and sterilization requirements
- Mixer is clean running and is suitable for general mixing, heat transfer and shear sensitive applications.
- Reduced bioburden
- Lower cost of maintenance
- Diamond coated mixer bearings ensure long life and optimum performance.
- Ability to mix the "last drop", ensures complete product recovery

Unparalleled Ultrafiltration

Plug and Play

The Pellicon® Process-scale Holder is uniquely designed to reduce the time required to install and remove TFF cassettes at production scale while keeping the flow path unchanged.

The holder can be configured with a manual or hydraulic closure. Hydraulic closure can be done with a hand pump or with an automated hydraulic box which allows local or distant control.



Benefits:

- Compact footprint
- TFF cassettes can be installed/removed quickly
- Easy to vent and fully drainable, maximizes product recovery
- Easy retrofit from manual to hydraulic closure
- Flow path unchanged, minimizes future re-qualification and validation effort in new process applications

Air Integrity Test

In order to ensure that the cassettes have been installed properly and has not sustained any damage during storage and handling, we recommend integrity testing prior to startup and after each post use cleaning. Air Integrity Test accessories consist of a set of air pressure regulators and fittings including assembly procedure to guarantee an easy plug and play solution.

Pellicon® 3 Ultrafiltration Cassettes

The tangential flow filtration cassette of choice for demanding filtration processes requiring unbeatable performance consistency. For use in applications including: monoclonal antibodies, recombinant and non-recombinant proteins, albumin, hormones, vaccines, and growth factors.

Biomax® membrane

Pellicon® 3 cassettes with Biomax® membranes are designed for the filtration of therapeutic proteins, albumin, hormones, vaccines and growth factors. These advanced, high-performance cassettes are ideal for today's processes that require higher operating pressures, temperatures and higher caustic cleaning regimes.

Ultracel® membrane

Pellicon® 3 Cassettes with Ultracel® membrane are the device of choice for today's higher titer therapeutic antibodies as well as the more demanding filtration processes that require low protein fouling. The new D screen is optimized for applications that require higher viscosity and concentration applications.

Benefits:

- Robust, void-free membranes for optimum product recovery and performance consistency
- All thermoplastic design, protective end cap and integrated gasket provides great process consistency and ease of use
- Predictable and fast process scalability from lab to production scale
- Robust product design ideally suited to filtration processes with higher operating pressures, temperatures and caustic cleaning regimes
- Automated manufacturing delivers unbeatable performance consistency and reliability
- Proven process expertise and technical support to partner with you from development to full scale manufacturing
- Optimized flow path for higher flux and resolution separation capability

Provantage® Bioprocess Consulting Services

Provantage® Bioprocess Consulting Services leverage our core expertise, products, services and technology in downstream production to help solve your business problem or challenge. Our commitment to your project outcomes and timelines is managed with our stage gate approach and a dedicated project manager.

Application Expertise

Our Biomanufacturing Sciences Network (BSN) is a global team of over 85 engineers, scientists and technology specialists who provide expertise and peer-to-peer support in process development and manufacturing. We act as an extension of your team, helping you to minimize potential risk and streamline your operations. With over 3,000 client engagements, our toolkit of best practices will ensure your project is delivered on time and within budget.

Design and Implement

From lab-scale to pilot and manufacturing facility start-up, EMD Millipore is a partner of choice for providing consultative expertise on current best practices to integrate device, hardware and process technology, and process automation. We can provide consultative evaluations for TFF optimization and operating strategies.

Develop

With our 35+ year history manufacturing and implementing TFF technologies, EMD Millipore application specialists develop reproducible, scalable and robust TFF processes that meet your specific requirements and your required scale.

Optimize

Starting with a comprehensive technical assessment and characterization of your existing TFF step, EMD Millipore application specialists can recommend and implement TFF enhancements that use best-practice operating conditions and state of the art processes to deliver an optimized and validatable TFF process at your targeted scale, in a timely manner.

Transfer

During the lifecycle of a biopharmaceutical, technical transfers occur at various stages: from research to clinical development to commercial manufacturing, and from one manufacturing facility to another. EMD Millipore leverages experienced technical staff, strong project management, and good documentation practices on both sides throughout the course of transfer activities to ensure a robust and successful transfer.

Troubleshoot

EMD Millipore has extensive experience in troubleshooting and investigating manufacturing, method and process development issues. Our experienced team works together collectively with your technical project team to identify the root cause and to develop a robust, acceptable path forward.

Provantage® implementation services

In the biopharmaceutical industry, implementing new equipment with respect to Quality rules and guidelines can be challenging. To help you stay ahead in today's demanding and competitive production environment, our Provantage® Services group provides unparalleled support for implementation of the Cogent® Process Scale System. With a wide range of comprehensive packages to meet your unique manufacturing requirements, resulting in peace of mind and maximum operational flexibility.

	SAT and IQ/OQ	Operator training	CCP® Software Design	CCP® Software Training	Support for PQ
Qualification package GMP	•	•			•
Single Molecule cGMP package	•	•	•		•
Full cGMP package	•	•	•	•	•

Benefits:

- Qualify your system with our IQ/OQ service protocols and use our qualified Field Service Engineers with years of product experience to ensure your system functions as specified in cGMP environments
- Train your operators with an interactive, hands-on courses for either system operation, or advanced CCP® software recipe creation training by certified trainers
- Get the support of our experienced Biomanufacturing Engineers during your Process Performance Qualification
- Maintain your system with annual preventive maintenance by qualified Field Service Engineers to ensure the lifetime of the system and ultimately reduce your capital expenditures

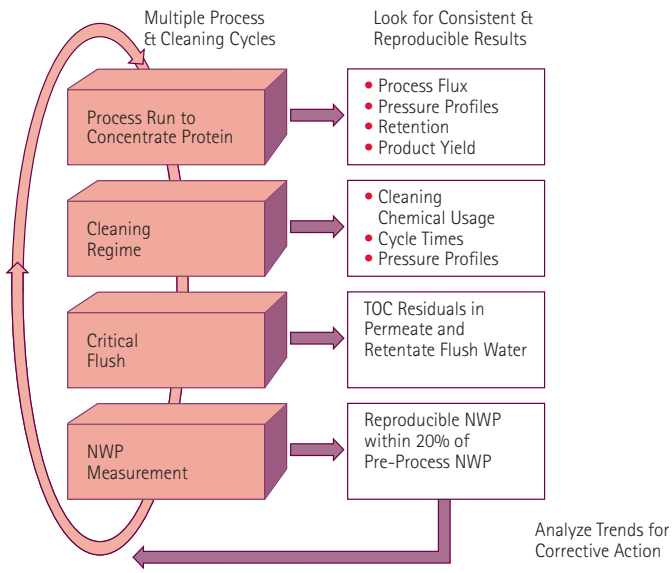
Provantage® Lab Services

Establishing an effective cleaning and sanitization plan for equipment used is a fundamental cGMP requirement necessary to assure the quality and consistency of your drug substance. Effective and consistent membrane cleaning and sanitization after each process cycle is the single most important factor in maintaining system performance.

Cleaning and sanitization after every cycle removes residual foulants and contaminants from the membrane, preventing batch-to-batch carry over, maintaining optimal performance and maximizing the useful life of the filter cassettes.

Effectiveness is measured by the ability to control and eliminate microbial contamination, and to remove process foulants to restore membrane performance such that consistent flux and separation are achieved batch after batch.

Our Provantage® TFF Cleaning Services can help you develop cleaning and sanitization procedures that assure the safety and purity of your product and maximize the useful life of your TFF cassettes.



To place an order or receive technical assistance

In the U.S. and Canada, call toll-free 1-800-645-5476

For other countries across Europe and the world, please visit: **www.emdmillipore.com/offices**

For Technical Service, please visit: **www.emdmillipore.com/techservice**

EMD MILLIPORE

www.emdmillipore.com/offices

Lit. No. DS6445EN00 Rev. A 04/2015 PS-14-10900 Printed in USA.

MILLIPORE

- *Leading-edge void-free membranes to match virtually any separation challenge*
- *Short flow path for higher flux and higher resolution separation capability*
- *Choice of flow channel configuration providing process optimization capability*
- *Predictable, fast, scale-up*
- *True linear scalability from laboratory size modules to industrial assemblies for processing thousands of liters*

DATA SHEET

Pellicon® 2 Filters and Holders

High-performance tangential flow filters for biopharmaceutical process development, scale-up/scale-down and concentration/ purification/cell harvesting applications

Typical Applications

Concentration, desalting or buffer exchange of:

- Protein solutions
- Polysaccharide solutions
- Virus suspensions

Harvest, washing or clarification of:

- Cell cultures and lysates
- Colloidal suspensions
- Viral cultures

Superior TFF Performance

For research, process development, scale-up and production, Pellicon 2 filters and holders offer the following benefits:

Consistent High Flux and High Product Recovery

Millipore's Biomax® polyethersulfone and Ultracel® PLC-composite regenerated cellulose membranes have void-free structures that guard against leakage of solutes through microdefects normally associated with voids beneath the thin skins of conventional UF membranes (Figures 1 and 2).

These void-free membranes are more permeable, resulting in high-flux with equivalent or superior product retention (Figure 3). These void-free membranes provide the advantages of fast, high yield processing and smaller systems.

The long established Durapore® hydrophilic PVDF microfiltration membrane is well known for its exceptional combination of high flux, low protein binding and high product recoveries.

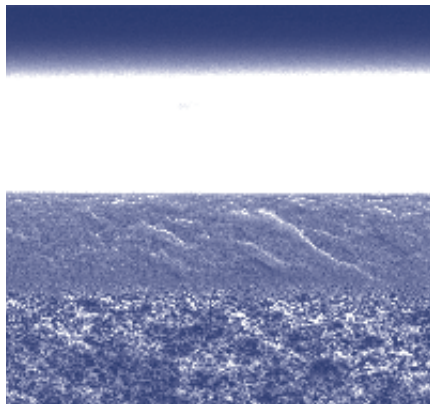


Figure 1. *Void-free Biomax 10 modified polyethersulfone membrane*

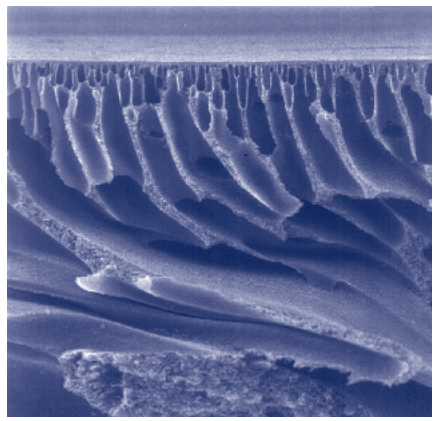


Figure 2. *Conventional 10 kD polyethersulfone membrane with sub-surface voids*

Easy, Reliable Linear Scale-Up from the Lab to the Production Plant

Pellicon 2 Mini filters scale-up easily and reliably from the laboratory to the production plant (Figures 4 and 5). By ensuring every flow channel has the same length, height and turbulence promoter as well as flow direction and materials of construction, we maintain the same ultrafilter/microfilter performance at all scales. Thus, rapid and reliable translation of processes from lab to manufacturing scale is easily achieved.

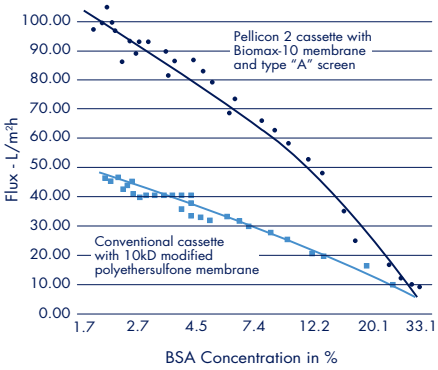
Linear Scale-Up

Mini filters (0.1 m^2/1.1 ft^2) and holders are designed for laboratory ultrafiltration/microfiltration of 100 mL to 10 L volumes, yet scale up linearly to Pellicon 2 Cassette (0.5 m^2/5.4 ft^2) and Maxi (2.5 m^2/26.9 ft^2) filters used in the pilot or manufacturing plant to process volumes from one liter to thousands of liters.

Thus, whether you operate 0.1 m^2 or 100 m^2 of installed area, every Pellicon 2 filter operates with the same pressure drop, flow velocity and concentration profile for true, rapid and simple linear scale-up.

Pellicon 2 Filters Proof of Performance

Improved Flux



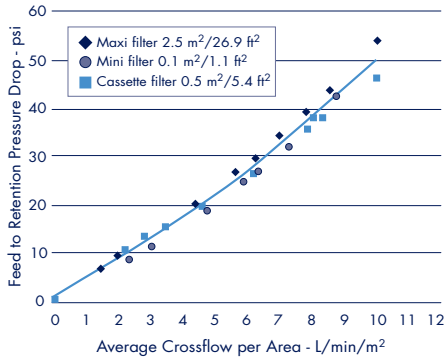
Feed pressure: 5.6 bar/80 psi
Retentate pressure: 2.1 bar/30 psi
Temperature: 10 – 13.5 °C
Initial volume 28 L
Final volume: 2 L

Conclusion

Pellicon 2 filters with Biomax membranes provide up to two-times the process flux of conventional cassettes resulting in faster processing and smaller systems.

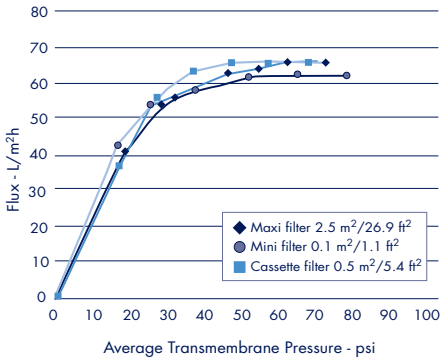
Figure 3. *Flux versus BSA concentration*

Linear Scalability



Temperature: 8 °C

Figure 4. *Feed to retentate pressure drop versus average crossflow on a 10% BSA solution*



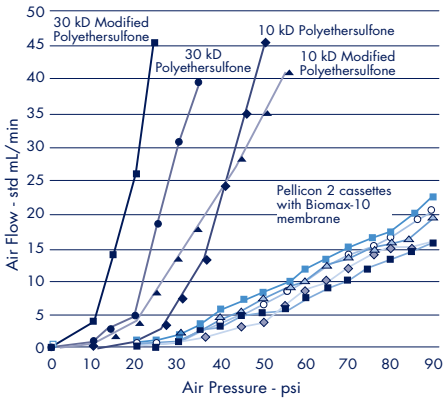
Temperature: 8 °C
Feed to retentate pressure drop: 2.8 bar/40 psi

Conclusion

(Figures 4 and 5) Pellicon 2 family of cassette filters scale linearly from 0.1 to 0.5 to 2.5 m^2 (1.1 to 5.4 to 26.9 ft^2) sizes for rapid, accurate and safe process scale-up and transfer.

Figure 5. *Flux versus average transmembrane pressure on a 10% BSA solution.*

Improved Reliability



Conclusion

The void-free structure of Biomax membranes is demonstrated by low, linear air diffusion values. This performance ensures better process reliability and safety and better product retention for higher yields.

Figure 6. *Integrity test comparison-air flow through wetted cassettes*

Greater Process Reliability and Reproducibility

The combination of defect-free membranes with Millipore's highly reliable manufacturing processes, offers greater consistency of process parameters.

The high quality of Millipore's ultrafiltration membranes is further ensured by our pioneering multiple-solute mixed-dextran retention profile test. Unlike the single solute protein retention test, Millipore's retention profile test measures and ensures reproducible retention performance of our UF membranes over the entire range of molecular weights retained by the membrane, not just at one or two molecular weights.

Low Product Loss

Pellicon 2 filters have a low minimum working volume – as low as 175 mL of retentate volume per square meter of membrane area. This low retentate volume permits high concentration factors to be reached with low starting volumes and maximizes the recovery of small sample volumes.

To prevent product loss, Pellicon 2 filters are 100% tested in manufacturing to ensure that every filter is integral.

In addition, Biomax and Ultracel membranes are exposed to a new high-pressure integrity test that provides greater sensitivity. The integrity test procedure and specifications are supplied so users can confirm integrity at high pressure when the filter is installed (Figure 6).

Biocompatibility

All wetted parts have been tested and meet the requirements of the USP Class VI biological test for plastics.

Superior Filter Quality

Pellicon cassettes are subjected to a complete array of quality control release tests.

A Certificate of Quality is included with every cassette.

Each casette is identified with a unique serial number.

Validatable

Since 1973, Pellicon filters and systems have been successfully used for development and scale-up of processes for manufacturing injectable protein and polysaccharide drugs, in the serum fractionation, biotechnology, vaccine and pharmaceutical industries.

Pellicon 2 filters and systems were developed based upon Millipore's experience serving these applications, and are supported by an extensive Validation Support Data Package proving performance claims and demonstrating the suitability of these filters for drug manufacturing in validated processes. This package is available upon request.

Millipore can further assist your validation efforts through:

- Design and fabrication of standard and custom turnkey TFF systems for drug manufacturing facilities
- Installation and operational qualification services for these systems
- Validation support services for tangential flow filter use in drug manufacturing processes.
- Training on TFF process scale-up, optimization and development.

A Choice of Feed Channel Screens

For optimal performance in a range of applications Pellicon 2 filters incorporate three types of feed-channel screens:

- *Type A screen (tight screen)* is optimized to operate Biomax membranes with maximum flux with low-viscosity solutions.
- *Type C screen (coarse screen)* is optimized to operate PLC series membranes with maximum flux. The Type C screen is also available with Biomax-50, 100, 300, 500 and Biomax 1000 membranes for concentration and diafiltration of viscous solutions.
- *Type V screen (open channel)* is optimized for very viscous solutions or solutions with higher levels of suspended solids.

Normalized Recirculation Rates

Parameter	Unit	Typical ΔP		
Screen Type		A	C	V
Recirculation Rate	L/min/m^2	4/6	5/35	
Differential Pressure	bar/psi	1.4/20	0.4/6	

Screen Selection Guidelines

Solution Type	Screen Type
Dilute protein solution or low viscosity solutions (MAbs, interferons)	A screen (tight screen)
Concentrated protein solutions or high viscosity solutions (IgG, biopolymers)	C screen (course screen)
High viscosity solutions (polysaccharides, certain microfiltration or clarification applications)	V screen (loose screen)

For More Detailed Information

Request literature number P17512 – User Guide for Pellicon Filters.

Specifications

Temperature Range

Mini, Cassette and Maxi:
4 to 50 °C

Maximum Forward Transmembrane Pressure

Device Size (m^2)	Biomax	Ultracel
0.1	6.8 bar (100 psi) Max	6.8 bar (100 psi) Max
0.5	6.8 bar (100 psi) at 30 °C	3.4 bar (50 psi) at 30 °C
2.5	6.8 bar (100 psi) at 30 °C	3.4 bar (50 psi) at 30 °C

Maximum Reverse Transmembrane Pressure

Device Size (m^2)	Biomax	Ultracel
0.1	0.33 bar (5 psi)	0.33 bar (5 psi)
0.5	0.33 bar (5 psi)	0.33 bar (5 psi)
2.5	0.33 bar (5 psi)	0.33 bar (5 psi)

Prefiltration Required

Mini, Cassette and Maxi:
100 µm

Dimensions

Device	Width	Length	Thickness
Mini	5.6 cm	21 cm	1.5 cm (V screen-2.16 cm)
Cassette	17.8 cm	21 cm	1.5 cm (V screen-2.16 cm)
Maxi	17.8 cm	21 cm	7.6 cm (V screen-9.0 cm)

Membrane Selection Guideline

Membrane Type	Materials	Benefits
Biomax	Modified polyethersulfone	Highest flux ultrafiltration membrane Excellent chemical resistance Void-free structure for higher yield and reliability
Ultracel PLC	Regenerated cellulose (ideal for protein solutions < 20 g/L) PLC membranes are composite membranes cast on a microporous substrate for defect-free membranes with superior adhesion. Brings higher resolution, improved yields and superior back-pressure resistance	Extremely low protein binding hydrophilic membrane Highest product recovery and improved performance with difficult to process streams (antifoams, lipids, protein transmission applications)
Durapore	Hydrophilic PVDF	Very hydrophilic microporous membrane for cell harvest or clarification applications

Pellicon 2 Membrane Selection Chart

Approximate Molecular Weight (range of solutes retained >99%, kD)		Membrane	NMWL (kD) or Microns	Membrane Material	pH Range
High Flux Biomax Membranes – Void-free for Higher Yield and Reliability					
12 – 25	(growth factors, hormones)	Biomax-5	5	modified polyethersulfone	1 – 14
25 – 50	(growth factors, hormones)	Biomax-8	8	modified polyethersulfone	1 – 14
50 – 100	(albumin, hemoglobin)	Biomax-10	10	modified polyethersulfone	1 – 14
100 – 140	(enzymes)	Biomax-30	30	modified polyethersulfone	1 – 14
140 – 300	(IgG's)	Biomax-50	50	modified polyethersulfone	1 – 14
300 – 500	(small viruses and antigens)	Biomax-100	100	modified polyethersulfone	1 – 14
>500	(IgM's, large viruses)	Biomax-300	300	modified polyethersulfone	1 – 14
>0.03 µm	(large viruses, colloids, particulates)	Biomax-500	500	modified polyethersulfone	1 – 14
>0.03 µm	(large viruses, cells, colloids, particulates)	Biomax-1000	1000	modified polyethersulfone	1 – 14
Ultracel PLC Series – for High Recoveries					
8 – 18	(proinsulin, hematopoetic factors)	PLCCC	5	regenerated cellulose	2 – 13
18 – 60	(hemoglobin, enzymes)	PLCGC	10	regenerated cellulose	2 – 13
60 – 200	(monoclonal IgG's)	PLCTK	30	regenerated cellulose	2 – 13
200 – 500	(small viruses, viral antigens)	PLCHK	100	regenerated cellulose	2 – 13
>500	(large viruses, IgM's)	PLCMK	300	regenerated cellulose	2 – 13
>0.03 µm	(large viruses, cells, colloids, particulates)	PLCXK	1000	regenerated cellulose	2 – 13
Durapore Membranes – for Microporous Applications					
Clarify cell lysates and protein solutions, clarify viral cultures		VVPP	0.1 µm	hydrophilic PVDF	2 – 11
Harvest & wash colloidal suspensions, bacterial cells; clarify protein solutions and viral cultures		GVPP	0.22 µm	hydrophilic PVDF	2 – 11
Harvest & wash colloidal suspensions, cell & viral cultures, clarify protein solutions & viral cultures		HVMP	0.45 µm	hydrophilic PVDF	2 – 11
Harvest cell cultures or colloidal suspensions		DVPP	0.65 µm	hydrophilic PVDF	2 – 11

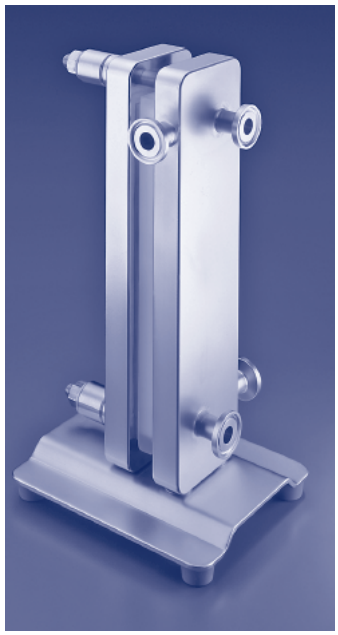
Ordering Information

Pellicon 2 Filters

	Filters with A Screens (Tight Screen)			Filters with Type C Screens (Coarse Screen)		
Membrane	**0.1 m²/1.1 ft²**	**0.5 m²/5.4 ft²**	**2.5 m²/26.9 ft²**	**0.1 m²/1.1 ft²**	**0.5 m²/5.4 ft²**	**2.5 m²/26.9 ft²**
Biomax Series – Modified Polyethersulfone						
Biomax 5	P2B0 05A 01	P2B0 05A 05	P2B0 05A 25	+	+	+
Biomax 8	P2B0 08A 01	P2B0 08A 05	P2B0 08A 25	+	+	+
Biomax 10	P2B0 10A 01	P2B0 10A 05	P2B0 10A 25	+	+	+
Biomax 30	P2B0 30A 01	P2B0 30A 05	P2B0 30A 25	+	+	+
Biomax 50	P2B0 50A 01	P2B0 50A 05	P2B0 50A 25	P2B0 50C 01	P2B0 50C 05	P2B0 50C 25
Biomax 100	P2B1 00A 01	P2B1 00A 05	P2B1 00A 25	P2B1 00C 01	P2B1 00C 05	P2B1 00C 25
Biomax 300	+	+	+	P2B3 00C 01	P2B3 00C 05	P2B3 00C 25
Biomax 500	+	+	+	P2B5 00C 01	P2B5 00C 05	P2B5 00C 25
Biomax 1000	+	+	+	P2B0 1MC 01	P2B0 1MC 05	P2B0 1MC 25
Ultracel PLC Series – Regenerated Cellulose, Composite Construction						
5 kD	NA	NA	NA	P2C0 05C 01	P2C0 05C 05	P2C0 05C 25
10 kD	NA	NA	NA	P2C0 10C 01	P2C0 10C 05	P2C0 10C 25
30 kD	NA	NA	NA	P2C0 30C 01	P2C0 30C 05	P2C0 30C 25
100 kD	NA	NA	NA	P2C1 00C 01	P2C1 00C 05	P2C1 00C 25
300 kD	NA	NA	NA	P2C3 00C 01	P2C3 00C 05	P2C3 00C 25
1000 kD	NA	NA	NA	P2C0 1MC 01	P2C0 1MC 05	P2C0 1MC 25
Durapore – Hydrophilic PVDF						
0.1 µm	+	+	+	P2VV PPC 01	P2VV PPC 05	P2VV PPC 25
0.22 µm	+	+	+	P2GV PPC 01	P2GV PPC 05	P2GV PPC 25
0.45 µm	+	+	+	P2HV MPC 01	P2HV MPC 05	P2HV MPC 25
0.65 µm	+	+	+	P2DV PPC 01	P2DV PPC 05	P2DV PPC 25

Each Pellicon filter is packed one per box and includes Operating Instructions. A Certificate of Quality is included in every box.
Silicone intercassette gaskets are required for use with Pellicon 2 filters. Two gaskets are packed in the box with every Pellicon 2 filter.
+ = On request (custom order)
NA = not available

Filters with V Screens (Loose Screen)		
0.1 m²/1.1 ft²	**0.5 m²/5.4 ft²**	**2.0 m²/21.5 ft²**
P2B0 05V 01	P2B0 05V 05	P2B0 05V 20
P2B0 08V 01	P2B0 08V 05	P2B0 08V 20
P2B0 10V 01	P2B0 10V 05	P2B0 10V 20
P2B0 30V 01	P2B0 30V 05	P2B0 30V 20
P2B0 50V 01	P2B0 50V 05	P2B0 50V 20
P2B 100V 01	P2B1 00V 05	P2B1 00V 20
P2B3 00V 01	P2B3 00V 05	P2B3 00V 20
P2B5 00V 01	P2B5 00V 05	P2B5 00V 20
P2B0 1MV 01	P2B0 1MV 05	P2B0 1MV 20
P2C0 05V 01	P2C005V 05	P2C0 05V 20
P2C0 10V 01	P2C0 10V 05	P2C0 10V 20
P2C0 30V 01	P2C0 30V 05	P2C0 30V 20
P2C1 00V 01	P2C1 00V 05	P2C1 00V 20
P2C3 00V 01	P2C3 00V 05	P2C3 00V 20
P2C0 1MV 01	P2C0 1MV 05	P2C01MV 20
P2VV PPV 01	P2VV PPV 05	P2VV PPV 20
P2GV PPV 01	P2GV PPV 05	P2GV PPV 20
P2HV MPV 01	P2HV MPV 05	P2HV MPV 20
P2DV PPV 01	P2DV PPV 05	P2DV PPV 20



Pellicon 2 Mini Holder

Pellicon 2 Mini holder operates one to three Mini filters in parallel for total areas of 0.1 to 0.3 m² (1.1 – 3.3 ft²). This sanitary holder is tightened with a small torque wrench to compress the filters between a manifold plate that conveys fluids in and out of the filters and an end plate that seals the filters together. The Mini holder is designed for process development and small volume pharmaceutical manufacturing.

Materials of Construction

Manifold and End Plates:
316 L stainless steel

Base, Tie Rods, Spacers and Washers:
304 stainless steel

Feet:
Thermoplastic rubber

Gaskets:
Silicone

Nuts:
Silicone bronze

Separator Plates

An optional separator plate allows processing simultaneously with up to three 0.1 m²/1.1 ft² cassettes to determine the best molecular weight cut-off in a single study on the same feed material.

Connections

All manifold connections are standard ½-inch sanitary clamp type.

Operating Parameters

Temperature Range:
4 to 50 °C. The Mini holder can be autoclaved without filters installed. The filters themselves cannot be autoclaved.

Maximum Pressure:
6.8 bar

Dimensions

Height: 260 mm; *Width:* 114 mm

Length: 140 mm; *Weight:* 5 kg

Holder Manifold Volume:

Feed plus retentate: 5.3 mL

Permeate: 6.4 mL

Stainless Steel Pellicon Holder

XX42P0080

The stainless steel Pellicon filter holder, designed for sanitary applications, can be used alone or to expand existing cassette ultrafiltration (CUF) systems or to replace existing holders.

It requires only to be connected to an existing sanitary pump and piping for tangential flow microporous filtration or ultrafiltration.

It can accomodate up to 5 m^2/55 ft^2 filter area as shipped with long tie rods or 0.5 to 2.5 m^2 (5.4 – 26.9 ft^2) with accessory short tie rods.

Materials of Construction

Wetted Surfaces:
316 L stainless steel

Non-wetted Surfaces:
Silicon bronze nuts

Dimensions

Length: 28 cm; *Width:* 19 cm

Height: 25 cm

Operating Parameters

Operating Temperature Range:
4 to 50 °C. The Pellicon holder can be autoclaved without pressure gauges and filters; holder with gauges cannot be steamed. Pellicon filters cannot be steamed or autoclaved.

Connections

Sanitary ¾" TC connections;
1½" TC connections for gauges.

Shipping Weight

24 kg

Process-scale Pellicon Holder

The Pellicon Process-scale Holder is a unique innovation for production scale Pellicon systems. This holder, vertically mounted, can hold up to 80 m^2/880 ft^2 of membrane area.

Benefits

- Extremely compact footprint
- Easy to change cassettes
- Easy to vent and fully drain
- Simple connections
- Up to 4 levels. Can be easily extended in levels for simple membrane area expansion
- Each level up to 20 m^2/220 ft^2
- Uses standard and Maxi Cassettes
- Can be adapted for series or parallel configurations
- Simplifies pipework connection
- Hydraulic closure systems are available for the stainless-steel Pellicon holder and the process-scale Pellicon holder. These systems are convenient, reliable and easy to use to enable rapid and repeatable loading operation and storage of Pellicon 2 cassettes.

Materials of Construction

Manifold segment, fitting blocks and end plate 316 L stainless steel; tie rods 304 and 304 L stainless steel.

Ordering Information

Pellicon 2 Filter Holders

Description	Catalogue No.
Pellicon 2 Mini filter holder	XX42 PMI NI
Pressure gauges One diaphragm-protected digital pressure gauge, 0 – 7 bar, ¾-inch fittings	XX42 PSG 01L
Pressure gauge adapters	XX42 PM0 01
Fitting kit Contains all tees, clamps, gaskets and a valve to connect tubing and pressure gauges to the Pellicon 2 Mini holder	XX42 PFK 01
Pellicon filter holder (for cassettes and Maxi filters)	XX42 P00 80
Pellicon 2 double thick gasket	PSSP 2XC 10
Pellicon Process-scale holder support and plate	XX42 SSP LT
Pellicon Process-scale holder	On request

To Place an Order or Receive Technical Assistance

For additional information call your nearest Millipore office:
In the U.S. and Canada,
call toll-free **1-800-MILLIPORE (1-800-645-5476)**
In the U.S., Canada and Puerto Rico, fax orders to **1-800-MILLIFX (1-800-645-5439)**
Outside of North America contact your local office. To find the office nearest you visit **www.millipore.com/offices.**
Internet: **www.millipore.com**
Technical Service:
www.millipore.com/techservice

MILLIPORE

A Typical Pellicon Production Processing System

Millipore supplies a range of standard and custom engineered systems. These systems can contain from 1 m^2/11 ft^2 to several hunded m^2 of membrane area, with Clean-in-Place (CIP) or Steam-in-Place (SIP) integrated as appropriate. Systems can also be supplied with integrated process vessels in manual or fully automatic versions.

All systems are designed, engineered and manufactured in ISO® 9001 registered facilities, and are supplied with extensive validation data support packages.

Please contact us to discuss your specific application and process requirements.

Pellicon XL Devices for Process Development

For process development of volumes from 50 mL to 1 liter, Millipore offers Pellicon XL devices. This small volume TFF filter is designed for true scalability by providing the same flow path, channel length, and channel height as the Pellicon 2 cassettes. Based on proven TFF membrane technology, Pellicon XL devices ensure reliable, consistent and predictable performance.

Lit. No. DS1210EN00 Rev. A 10/04
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GE Healthcare
Life Sciences

Capto™ S, Capto Q, and Capto DEAE

Capto S, Capto Q and Capto DEAE are, respectively, strong cation, strong anion and weak anion exchange media for packed bed chromatography that increase speed and throughput in capture and intermediate purification. They combine high capacity with high flow velocity and low backpressure to reduce process cycle times and increase productivity. As BioProcess™ media, the Capto range meets the demands of large-scale biopharmaceutical manufacturers by:

- Raising productivity with high dynamic binding capacity at high flow
- Reducing process time with high volume throughput
- Cost-effective processing with smaller unit operations

Chromatography media characteristics

High throughput in downstream purification requires separation media that combine mechanical strength of the matrix with a pore structure that allows fast mass transfer and high capacity for target molecules. Capto media are based on a highly rigid agarose base matrix that offers outstanding pressure/flow properties, optimized pore structure, and very high chemical stability to support CIP procedures. Capto media are intended for general use in large-scale bioprocess operations. The basic characteristics of Capto S, Capto Q, and Capto DEAE are summarized in Table 1.

High flow and low backpressure in large-scale columns

High flow velocities allow increased productivity of large-scale bioprocessing operations and processing of larger volumes in one working shift. Shorter cycle times also reduce exposure of the target protein to proteases. Typical flow velocities for Capto media in a 1 m diameter column with 20 cm bed height are over 700 cm/h, with a backpressure below 3 bar.

Figure 1 compares the pressure/flow performance of Capto with Sepharose 6 Fast Flow in a representative large-scale situation with a 1 m column that gives negligible wall support.

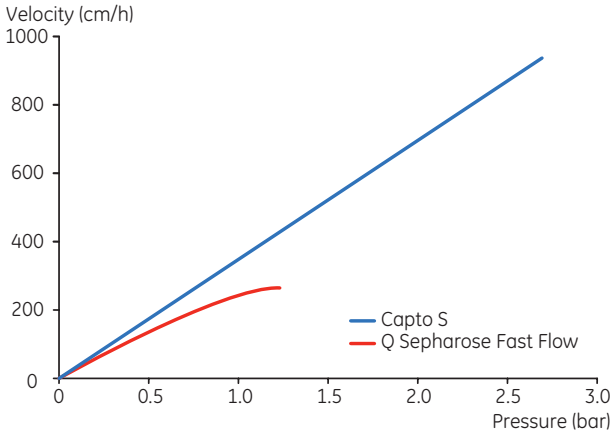


Fig 1. Pressure/flow curve for Capto S compared to Q Sepharose™ Fast Flow. *Running conditions*: AxiChrom™ 1000 for Capto S, Chromaflow™ 1000 for Q Sepharose Fast Flow, 20 cm packed bed, with water at 20°C. The pressure includes pressure drop from the bed and the column. System/tubing pressure is excluded.

Although the bead and pore sizes are similar between the two matrices, the pressure/flow properties of Capto are significantly better. This is a result of the exceptional mechanical stability of the Capto base matrix.

Anion and cation exchangers with fast mass transfer and high dynamic binding capacities

For ion exchange, Capto S uses a sulfonate group, Capto Q uses a quartenary amine group and Capto DEAE uses a diethylaminoethyl group. The groups are linked to a high flow agarose base matrix modified with a dextran surface extender which further increases capacities and mass transfer properties. Fast mass transfer ensures high dynamic binding capacity over a wide range of residence times. High binding capacity also contributes to shortening the overall processing time as the total number of cycles may be reduced. The dynamic binding capacities of Capto S, Capto Q and Capto DEAE at different residence times are shown in Figure 2.

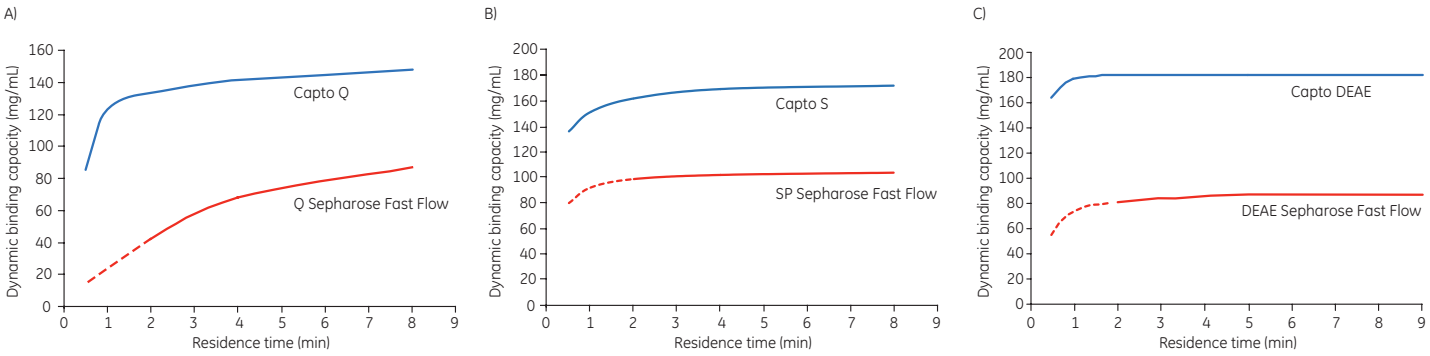


Fig 2. Dynamic binding capacity as a function of residence time for: A) Capto Q and bovine serum albumin (BSA), B) Capto S and α-chymotrypsin, C) Capto DEAE and amyloglucosidase. For Sepharose Fast Flow media, residence times below 2 min are not possible in large-scale columns.

Table 1. Characteristics of Capto S, Capto Q, and Capto DEAE

	Capto S	Capto Q	Capto DEAE
Matrix	highly cross-linked agarose with dextran surface extender		
Ion exchange type	strong cation, S	strong anion, Q	weak anion, DEAE
Charged group	$-SO_3^-$	$-N^+(CH_3)_3$	$-N^+H(CH_2CH_3)_2$
Total ionic capacity	0.11 to 0.14 mmol Na^+/mL medium	0.16 to 0.22 mmol Cl^-/mL medium	0.29 to 0.35 mmol Cl^-/mL medium
Particle size[1]	90 µm (d_{50v})	90 µm (d_{50v})	90 µm (d_{50v})
Flow velocity	at least 700 cm/h in a 1 m diameter column with 20 cm bed height at 20 °C using process buffers with the same viscosity as water at < 3 bar (0.3 MPa)		
Dynamic binding capacity	> 120 mg lysozyme/mL medium[2]	> 100 mg BSA/mL medium[3]	> 90 mg ovalbumin/mL medium[3]
pH stability[4]			
short term	3 to 14	2 to 14	2 to 14
working	4 to 12	2 to 12	2 to 9
long term	4 to 12	2 to 12	2 to 12
Working temperature[5]	4°C to 30°C	4°C to 30°C	4°C to 30°C
Chemical stability	all commonly used aqueous buffers, 1 M acetic acid, 1 M NaOH[6], 8 M urea, 6 M guanidine hydrochloride, 30% isopropanol and 70% ethanol		
Storage	20% ethanol + 0.2 M NaAc	20% ethanol	20% ethanol
Avoid	oxidizing agents, cationic detergents	oxidizing agents, anionic detergents	oxidizing agents, anionic detergents

1 d_{50v} is the median particle size of the cumulative volume distribution.

2 Dynamic binding capacity at 10% breakthrough as measured at a residence time of 1 min, 600 cm/h in a Tricorn™ 5/100 column with 10 cm bed height, in a 30 mM sodium phosphate buffer, pH 6.8.

3 Dynamic binding capacity at 10% breakthrough as measured at a residence time of 1 minute, 600 cm/h in a Tricorn 5/100 column with 10 cm bed height in a 50 mM Tris-HCl buffer, pH 8.0.

4 Short term pH: pH interval that the medium can be subjected to, for cleaning- or sanitization-in-place (accumulated 90–300 h at room temperature) without significant change in function.
Working pH: pH interval where the medium binds protein as intended or is needed for elution, without adverse long-term effect.
Long term pH: pH interval where the medium can be operated without significant change in function.

5 Low temperatures can decrease capacity of Capto S and Capto DEAE.

6 No significant change in ionic capacity and carbon content after 1 week storage in 1 M NaOH at 40°C.

Rigid media for cost-effective purification

The rigidity of Capto products allows improved process economics. Capto media characteristics allow a wider working range of flow velocities, bed heights and sample viscosities, all of which affect processing costs in a positive way. High flow velocities increase volume throughput and reduce process time, longer bed heights means smaller equipment and reduced footprint, and high flow processing of viscous samples means less dilution and shorter cycle times.

The available degree of freedom in process design for a medium can be illustrated as its "window of operation". Figure 3 shows schematically the ranges for key operating variables for Capto IEX and Sepharose 6 Fast Flow. Given a maximum allowed pressure, it predicts the allowable combinations of column bed heights and operating velocities. The pressure limits, shown as blue and red curves, are based on a 1 m diameter column and calculated from 20 cm bed height and maximum operating velocities of 700 and 250 cm/h, respectively. At this point, the pressure is 3 bar for Capto and 1.3 bar for Sepharose 6 Fast Flow. For Sepharose 6 Fast Flow, 1.3 bar represents the highest recommended operating pressure for this medium at this scale. For Capto, 3 bar corresponds to the maximum pressure for many low-pressure systems; the medium as such can normally be run to the maximum pressure rating of low and medium pressure columns.

The size of the area below the pressure limit curves represents the window of operation, or the available operating range for the respective medium. As shown in Figure 3, this is significantly larger for Capto than for Sepharose 6 Fast Flow based media, especially when bed heights increase to 20-30 cm or more. At these bed heights, Capto can still be run at flow velocities of 300-400 cm/h or more. Thus, the high mechanical stability of Capto allows practical and cost-effective use of smaller diameter columns.

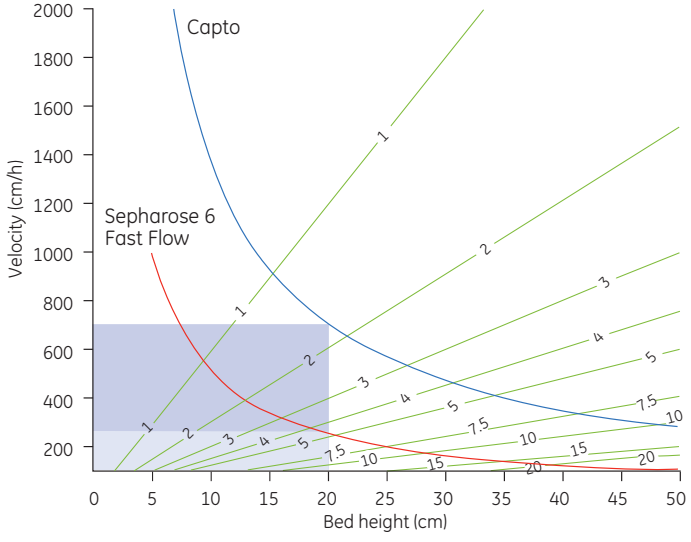


Fig 3. The highly rigid Capto base matrix allows a much larger window of operation (area below the curves) at large-scale than Sepharose 6 Fast Flow. This is particularly true at bed heights of 20-30 cm and above. Data correspond to a 1 m diameter column, at 20°C and viscosity of water. Red and blue curves correspond to pressure limits of 1.3 and 3 bar, respectively. Green contours give the residence time in the column in minutes.

A large window of operation also allows flexibility even if the viscosity of the feed is high. Doubling viscosity halves the operational velocity. For a feedstock with a viscosity of 2 cP at a bed height of 30 cm, the flow velocity of Capto is 235 cm/h compared to 80 cm/h for Sepharose 6 Fast Flow.

Figure 3 also shows contours of the residence time in the column. A long residence time allows for better utilization of the full equilibrium capacity. It is possible to increase the residence time by either decreasing the flow velocity, or increasing the column bed height. For Capto, increasing bed heights assures longer residence times even under high flow conditions.

Selectivity

The charged groups of the S, Q and DEAE ligands used in Capto media are identical to the charged groups used in many other ion exchange media. However, minor differences in selectivity can occur between media having the same ligand as illustrated in Figures 4 and 5. This is due to differences in base matrix, ligand density and surface extenders.

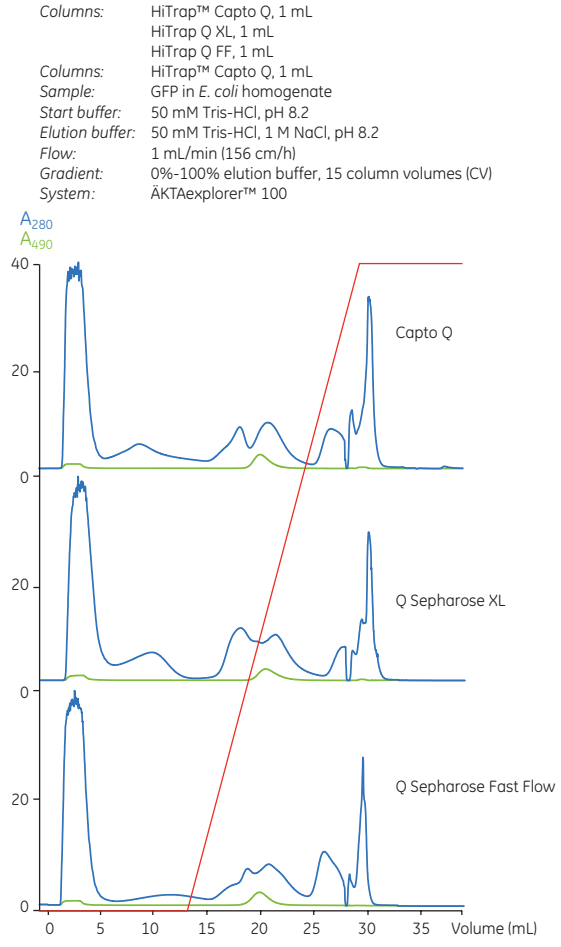


Fig 4. The separation ability of Capto Q for GFP compared to Q Sepharose Fast Flow and Q Sepharose XL media in 1 ml prepacked HiTrap columns.

Columns:	HiTrap Capto S, 1 mL HiTrap SP XL, 1 mL HiTrap SP FF, 1 mL
Sample:	α-chymotrypsin in *E. coli* homogenate
Start buffer:	50 mM Sodium acetate, pH 4.8
Elution buffer:	50 mM Sodium acetate, 1 M NaCl, pH 4.8
Flow:	1 mL/min (156 cm/h)
Gradient:	0% to 100% elution buffer, 10 CV
System:	ÄKTAexplorer 100

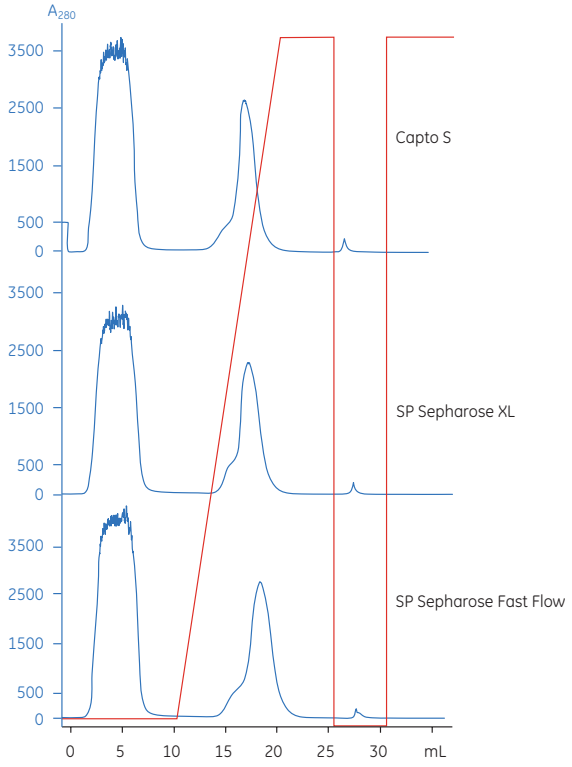


Fig 5. The separation ability of Capto S for α-chymotrypsin compared to SP Sepharose Fast Flow and SP Sepharose XL media in 1 mL prepacked HiTrap columns.

Strong vs weak ion exchangers

Strong ion exchangers like Capto S and Capto Q maintain their charge (and thus their function) over a wide pH range whereas with weak ion exchangers the degree of dissociation and thus ion exchange capacity varies with pH. Capto DEAE, although predominantly a weak anion exchanger, can not be fully discharged by raising the pH due to a minor content of quaternarized amine groups (Fig 6). It is therefore, possible to use DEAE media at higher pH values for separations of highly charged species as nucleotides, for example.

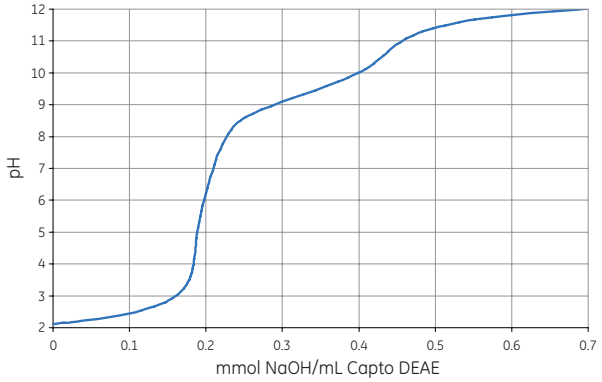


Fig 6. Titration curve of Capto DEAE.

Capto Q vs Capto DEAE

In addition to the difference in working pH range, the anion exchangers Capto Q and Capto DEAE also differ in selectivity. This difference, which is mainly pH dependent, is illustrated in Figures 7 and 8. Which product to chose depends on the individual application and what should be achieved during the separation. However the general recommendation is to start by evaluating the strong ion exchanger (Capto Q) since its function is less dependent on pH.

Column:	Tricorn 5/50, CV: 1 mL
Media:	Capto Q Capto DEAE
Sample :	Apo-transferrin (1.3 mg/mL) β-lactoglobulin (2.7 mg/mL) Pepsin (2 mg/mL)
Start buffer:	20 mM piperazine, pH 6.0
Elution buffer:	20 mM piperazine, 1 M NaCl, pH 6.0
Flow rate:	150 cm/h
Gradient:	0% to 80% elution buffer, 32 CV

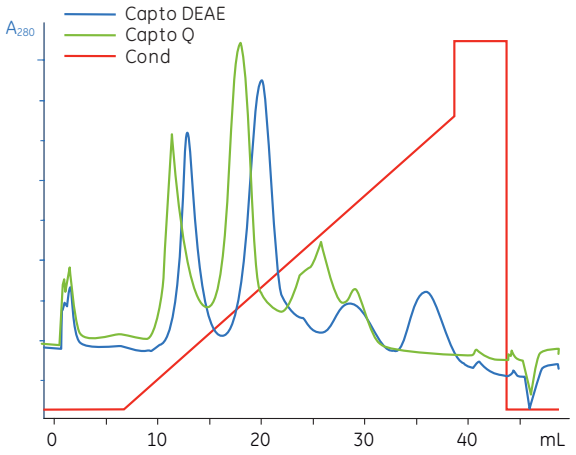


Fig 7. The selectivity difference between Capto Q and Capto DEAE at pH 6 exemplified by separation of a mixture containing three proteins and some breakdown products.

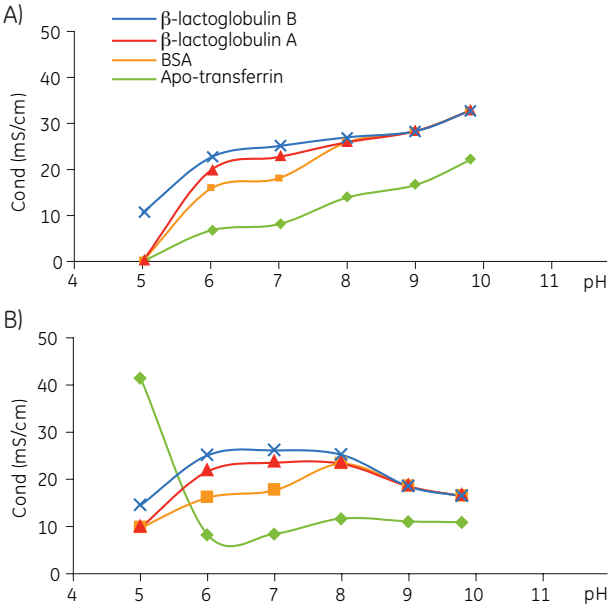


Fig 8. Elution conductivity as a function of pH for a set of model proteins on A) Capto Q, where only the change in surface charge of the proteins influences the elution position B) Capto DEAE, where both the change in surface charge of the proteins and the changed charge of the ligand determine the elution behavior.

Applications

Recent developments in upstream processing have resulted in larger feed volumes and increased protein expression levels. The combination of high volume throughput and high capacity makes Capto media the optimal choice for processing large amounts of protein in a fast and efficient way. As ion exchangers, their behavior can be easily controlled and application areas predicted by buffer choice and pI of the target proteins. Note that to reach the full potential of media where the design includes dextran, close attention must be paid to pH, conductivity, and other loading conditions. If this is done, very high capacities can be reached.

Note that the DEAE ligand has buffering properties. Therefore, a greater volume or concentration of equilibration buffer may be reqired for titration of the DEAE ligand in comparison to the non-titrateable Q ligand.

Improved productivity based on high flow features

Scale-up modelling and productivity calculations based on experimental data at small and pilot scale indicate that it is possible to capture and recover >100 kg of green fluorescent protein (GFP) from an *Escherichia coli* homogenate in 24 h using Capto Q in a 1.6 m i.d. column at 20 cm bed height (equivalent to 400 L of medium). Assuming the same process conditions, using Q Sepharose Fast Flow would require a 3 m i.d. column or 1400 L medium (in practice, this means three separate columns would be needed). This example supports the argument that Capto Q is being particularly suitable for high throughput and high productivity capture purification. For further details see Application note 11-0026-20.

Similar calculations indicate that it is possible to capture and recover >100 kg of α-chymotrypsin from *E. coli* homogenate in 24 hours with Capto S in a 0.8 m i.d. column at 20 cm bed height (equivalent to 100 L of medium). Assuming the same process cycle conditions, using SP Sepharose Fast Flow would require a 1.2 m i.d. column at 20 cm bed height (equivalent to 250 L medium). This example also indicates that Capto S is suitable for high throughput and high productivity capture purification. For further details see Application note 28-4078-15.

Process cycle times and productivity data for both examples are summarized in Table 3. Similar improvement in productivity is obtained with Capto DEAE compared to DEAE Sepharose Fast Flow.

Table 3. Results from scale-up modelling and productivity calculations for Capto Q, Capto S, and Capto DEAE as described in the text

Target protein and medium	Cycle time (min)	Productivity (kg/h, m³)	Media volume for 100 kg/24 h (L)
GFP			
Capto Q	91	11	400
Q Sepharose Fast Flow	190	3	1400
α-chymotrypsin			
Capto S	131	53	80
SP Sepharose Fast Flow	229	17	250
amyloglucosidase			
Capto DEAE†	197	37	114
DEAE Sepharose Fast Flow†	306	12	353

† Productivity calculations based on pure protein

Operation

Fast method development

In order to find the most suitable chromatography media and/or process conditions, screening and optimization should be performed. Time and sample can be saved in the early stages of development by using small-scale formats. PreDictor™ 96-well filter plates and Assist software may be used for initial screening of process conditions such as, pH and conductivity (Fig 9). ÄKTA™ avant – with Design of Experiment (DoE) functionality - or ÄKTAexplorer chromatography systems together with prepacked columns, such as HiScreen™ and HiTrap columns, can be used for further optimization and verification of the operating conditions.

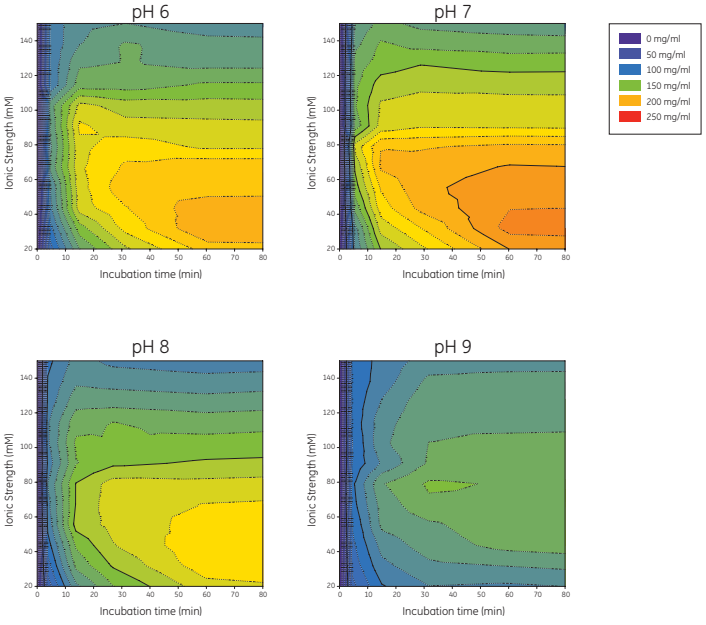


Fig 9. Screening for optimal binding conditions (pH, ionic strength and incubation time) for amyloglucosidase on Capto DEAE by batch uptake methodology using 96-well filter plates. Note that incubation time using this methodology is not equivalent to residence time in the column; typical residence times can be seen in Fig 2c.

UNICORN™ software on ÄKTA systems makes it simple to transfer the optimized method to a production scale process system.

For more information about method development and optimization, consult the handbooks, "High-throughput process development with PreDictor plates" and "Ion Exchange Chromatography & Chromatofocusing: Principles and Methods".

Fully scalable

Capto media belong to the BioProcess range of media that are developed and supported for production-scale chromatography. This includes validated manufacturing methods, secure supply and Regulatory Support Files (RSF) to assist process validation and submission to regulatory authorities.

Scale-up is typically done by keeping bed height and flow velocity constant, while increasing column bed diameter and flow rate. However, since optimization is preferentially done with small column volumes (to save sample and buffer), some parameters such as the dynamic binding capacity may be optimized using shorter bed heights than those being used in the final scale. As long as the residence time is constant, the binding capacity for the target molecule remains the same. Other factors, like clearance of critical impurities, may change when column bed height is changed and should be validated using the final bed height.

To utilize the full potential of Capto media, we recommend bed heights of 20 cm and higher at large scale.

A scale-up experiment was conducted for Capto S (Fig 10) using an optimized process for α-chymotrypsin with a constant residence time of 2 min. From Tricorn 5/100 the bed height was doubled to 20 cm in a XK 16/40 column (CV 40 mL). From the XK 16/40 column further scale up was conducted on an AxiChrom™ 50 (CV 400 mL) by increasing bed diameter to give a 200-fold scale up.

Cleaning and sanitization

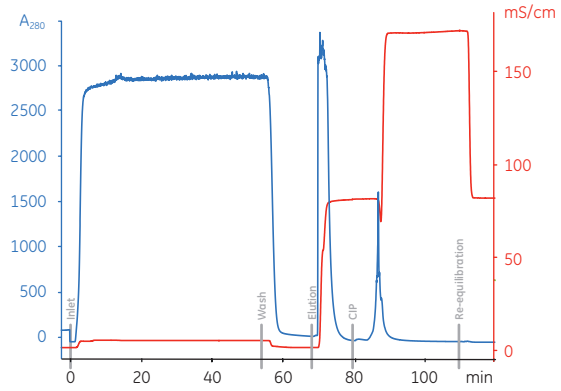
Cleaning-in-place (CIP) is a cleaning procedure that removes contaminants such as lipids, precipitates, or denatured proteins that may remain in the packed column after regeneration. Regular CIP also prevents the build-up of these contaminants in the media bed and helps to maintain the capacity, flow properties and general performance of the media.

A specific CIP protocol should be designed for each process according to the type of contaminants present. The frequency of CIP depends of the nature and the condition of the starting material, but one CIP cycle is generally recommended every 1 to 5 separation cycles. For some contaminants a more rigorous CIP procedure can be required for Capto DEAE than for Capto S and Capto Q, see instruction manual.

All Capto media withstand all standard CIP solutions (e.g. 1 M NaOH, 2 M NaCl or 70% ethanol) or combinations thereof.

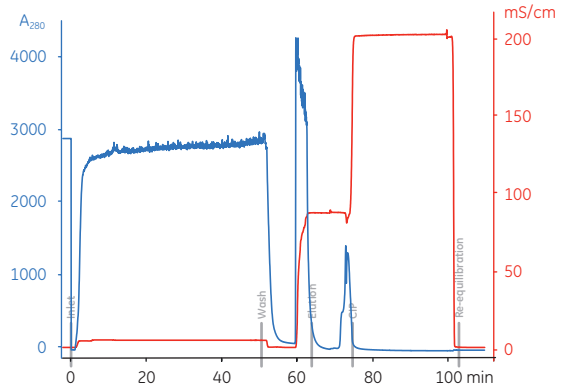
A)

Column:	Tricorn 5/100 (bed height 9.7 cm, CV=1.9 mL)
Medium:	Capto S
Sample:	α-chymotrypsin in *E. coli* homogenate, 4 mg/mL–50 mL
Start buffer:	50 mM NaAc, pH 4.8
Elution buffer:	50 mM NaAc, 1 M NaCl, pH 4.8
Flow rate:	285 cm/h
Gradient:	0%–100% 0 CV, 100% 5 CV
System:	ÄKTAexplorer 100
Residence time:	2 min



B)

Column:	XK 16/40 (bed height 20.7 cm, CV= 41.5 mL)
Medium:	Capto S
Sample:	α-chymotrypsin in *E. coli* homogenate, 4 mg/mL–1040 mL
Start buffer:	50 mM NaAc, pH 4.8
Elution buffer:	50 mM NaAc, 1 M NaCl, pH 4.8
Flow rate:	624 cm/h
Gradient:	0%–100% 0 CV, 100% 5 CV
System:	ÄKTAexplorer 100
Residence time:	2 min



C)

Column:	AxiChrom 50 (bed height 22 cm, CV= 431 mL)
Medium:	Capto S
Sample:	α-chymotrypsin in *E. coli* homogenate, 4 mg/mL–10.8 L
Start buffer:	50 mM NaAc, pH 4.8
Elution buffer:	50 mM NaAc, 1 M NaCl, pH 4.8
Flow rate:	645 cm/h
Gradient:	0%–100% 0 CV, 100% 5 CV
System:	ÄKTApilot™
Residence time:	2 min

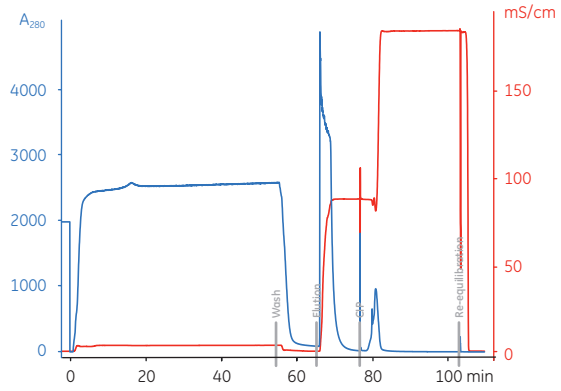


Fig 10. A 200-fold scale up using (A) Tricorn 5/100, (B) XK 16/40 and, (C) AxiChrom columns.

Equipment

Capto media can be used together with most equipment available for chromatography from lab scale to production scale. Due to the high rigidity of the medium, packing procedures are slightly different compared to Sepharose 6 Fast Flow based media. In process-scale, the preferred packing technique for Capto media is axial compression. Using AxiChrom columns, with Intelligent Packing and pre-set packing methods for all Capto media, is the most optimal and fastest approach. Appropriate columns from GE Healthcare are shown in Table 4. For details on packing lab-scale columns, see Instruction manuals, and for packing process-scale columns see Application notes.

All Capto media is also available in the ReadyToProcess™ platform, with pre-packed, pre-qualified and pre-sanitized ReadyToProcess columns ranging in size from 1-20 L.

Table 4. Appropriate columns

Column family range	Inner diameter (mm)
Lab scale:	
Tricorn	5, 10
HiScale™	16, 26, 50
Pilot and production scale:	
AxiChrom	50 – 1000
BPG	100 – 300†
Chromaflow	400 – 800‡

† The pressure rating of BPG 450 is too low to use it with Capto media.
‡ Larger pack stations might be required at larger diameters.

Storage

Capto S

Store unused media and prepacked columns at 4°C to 30°C in 20% in ethanol and 0.2 M sodium acetate.

Capto Q and Capto DEAE

Store unused media and prepacked columns at 4°C to 30°C in 20% in ethanol.

Ordering information

All Capto media are available as bulk media and in several pre-packed formats, including PreDictor 96-well filter plates, PreDictor RoboColumn™, HiTrap, HiScreen, and ReadyToProcess columns. Please contact your local GE Healthcare representative for additional information.

Product	Pack size	Code no.
Capto S	25 mL	17-5441-10
Capto S	100 mL	17-5441-01
Capto S	1 L	17-5441-03
Capto S	5 L	17-5441-04
Capto S	10 L	17-5441-05
Capto S	60 L	17-5441-60
Capto Q	25 mL	17-5316-10
Capto Q	100 mL	17-5316-02
Capto Q	1 L	17-5316-03
Capto Q	5 L	17-5316-04
Capto Q	10 L	17-5316-05
Capto Q	60 L	17-5316-60
Capto DEAE	25 mL	17-5443-10
Capto DEAE	100 mL	17-5443-01
Capto DEAE	1 L	17-5443-03
Capto DEAE	5 L	17-5443-04
Capto DEAE	10 L	17-5443-05
Capto DEAE	60 L	17-5443-60
Prepacked formats		
HiTrap Capto S	5 × 1 mL	17-5441-22
HiTrap Capto S	5 × 5 mL	17-5441-23
HiTrap Capto Q	5 × 1 mL	11-0013-02
HiTrap Capto Q	5 × 5 mL	11-0013-03
HiTrap Capto DEAE	5 × 1 mL	28-9165-37
HiTrap Capto DEAE	5 × 5 mL	28-9165-40
PreDictor AIEX screening, 20 µL	4 × 96-well filter plates	28-9432-89
PreDictor AIEX screening, 2 µL/6 µL	4 × 96-well filter plates	28-9432-88
PreDictor CIEX screening 20 µL	4 × 96-well filter plates	28-9432-91
PreDictor CIEX screening 2 µL/6 µL	4 × 96-well filter plates	28-9432-90
PreDictor Capto DEAE, 2 µL	4 × 96-well filter plates	28-9258-11
PreDictor Capto DEAE, 20 µL	4 × 96-well filter plates	28-9258-12
PreDictor Capto DEAE, 50 µL	4 × 96-well filter plates	28-9258-13
PreDictor Capto DEAE Isotherm	4 × 96-well filter plates	28-9432-80
PreDictor Capto Q, 2 µL	4 × 96-well filter plates	28-9257-73
PreDictor Capto Q, 20 µL	4 × 96-well filter plates	28-9258-06
PreDictor Capto Q, 50 µL	4 × 96-well filter plates	28-9258-07
PreDictor Capto Q Isotherm	4 × 96-well filter plates	28-9432-78
PreDictor Capto S, 2 µL	4 × 96-well filter plates	28-9258-08
PreDictor Capto S, 20 µL	4 × 96-well filter plates	28-9258-09
PreDictor Capto S, 50 µL	4 × 96-well filter plates	28-9258-10
PreDictor Capto S Isotherm	4 × 96-well filter plates	28-9432-79

Product	Pack size	Code no.
PreDictor RoboColumn Capto Q, 200 µl	One row of eight columns	28-9860-72
PreDictor RoboColumn Capto Q, 600 µl	One row of eight columns	28-9861-75
PreDictor RoboColumn Capto S, 200 µl	One row of eight columns	28-9860-81
PreDictor RoboColumn Capto S, 600 µl	One row of eight columns	28-9861-76
PreDictor RoboColumn Capto DEAE, 200 µl	One row of eight columns	28-9860-82
PreDictor RoboColumn Capto DEAE, 600 µl	One row of eight columns	28-9861-77
HiScreen Capto DEAE	1 × 4.7 mL	28-9269-82
HiScreen Capto Q	1 × 4.7 mL	28-9269-78
HiScreen Capto S	1 × 4.7 mL	28-9269-79
ReadyToProcess Capto Q	2.5 L	28-9017-23
ReadyToProcess Capto Q	10 L	28-9017-24
ReadyToProcess Capto Q	1 L	28-9510-90
ReadyToProcess Capto Q	20 L	28-9017-25
ReadyToProcess Capto S	20 L	28-9017-31
ReadyToProcess Capto S	2.5 L	28-9017-29
ReadyToProcess Capto S	10 L	28-9017-30
ReadyToProcess Capto S	1 L	28-9510-93

Related literature	Code no.
Data files	
PreDictor 96-well filter plates and Assist software	28-9258-39
PreDictor RoboColumn	28-9886-34
HiScreen prepacked columns	28-9305-81
ReadyToProcess columns	28-9159-87
BPG columns	18-1115-23
Chromaflow columns	18-1138-92
AxiChrom columns	28-9290-41
Application notes	
Capture of Green Fluorescent Protein on Capto Q	11-0026-20
Methods for packing Capto S and Capto Q in production scale columns	28-9259-32
High productivity capture of α-chymotrypsin on Capto S cation exchanger	28-4078-15
Screening and optimization of loading conditions on Capto S	28-4078-16
Screening of loading conditions on Capto S using a new high-throughput format, PreDictor plates	28-9258-40
Capto S cation exchanger for post-Protein A purification of monoclonal antibodies	28-4078-17
Process-scale purification of monoclonal antibodies – polishing using Capto Q	28-9037-16
Purification of a monoclonal antibody using ReadyToProcess columns	28-9198-56
Use of Capto ViralQ for the removal of genomic DNA from influenza virus produced in MDCK cells	28-9769-69
Two-step purification of monoclonal IgG_1 from CHO cell culture supernatant	28-9078-92
Handbooks	
High-throughput process development with PreDictor plates, principles and methods	28-9403-58
Ion Exchange Chromatography & Chromatofocusing: Principles and Methods	11-0004-21

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11-0025-76 AG 05/2012

Sartopore® 2 0.2 µm

Sterilizing Grade Filter Elements

Product Information

- Industry standard of high-performance liquid sterile filters
- Unique hydrophilic heterogeneous double layer Polyethersulfone membrane
- Exceptional high throughput and excellent flowrates at low pressure drops
- High thermal resistance and broad chemical compatibility

High-Performance and broad compatibility

Sartopore® 2 filter elements feature a unique hydrophilic heterogeneous double layer design of a 0.45 µm pre-filter and 0.2 µm final filter membrane with an exceptionally high throughput and flow-rate. In addition to its outstanding performance, the Polyethersulfone membrane gives Sartopore® 2 0.2 µm broad chemical compatibility, including a pH-range from pH 1 to pH 14, and a high thermal resistance.

Industry standard for sterile-grade liquid filters

Sartopore® 2 0.2 µm filters are fully validated as sterilizing grade filter elements according to current ASTM F-838 guidelines. Each individual element is integrity tested by diffusion and bubble point test prior to release, assuring absolute reliability. Sartopore® 2 filter elements are designed, developed and manufactured in accordance with an ISO 9001 certified Quality Management System. The Validation and Extractables Guide are available for compliance with regulatory requirements.

Scalability

Sartopore® 2 0.2 µm filter elements are available in a broad range of sizes and formats to provide linear scale-up from R&D to process scale. The wide range of membrane areas from 150 cm^2 to 1.8 m^2 per filter element guarantees greatest flexibility and most economic filter sizing.

Applications

- Therapeutics
- Biological Fluids
- Ophthalmic solutions
- Injectables
- Media
- SVPs, LVPs
- Antibiotics
- WFI
- Buffers
- Chemicals
- Cleaning and sanitizing agents
- Bulk pharmaceutical products

Technical Data

Available Sizes	Filtration Area	Max. Diffusion at 2.5 bar | 36 psi [ml/min]	Min. Bubble Point [bar | psi]
Cartridges, T-Style MaxiCaps® | MaxiCaps® | Gamma MaxiCaps®			
Size 0.5 (Only Cartridge)	0.3 m^2 | 3.2 ft^2	10	3.2 | 46
Size 1	0.6 m^2 | 6.5 ft^2	18	3.2 | 46
Size 2	1.2 m^2 | 12.9 ft^2	36	3.2 | 46
Size 3	1.8 m^2 | 19.4 ft^2	54	3.2 | 46
Mini Cartridges | MidiCaps® | Gamma MidiCaps®			
Size 7	0.05 m^2 | 0.5 ft^2	4	3.2 | 46
Size 8	0.1 m^2 | 1.1 ft^2	5	3.2 | 46
Size 9	0.2 m^2 | 2.2 ft^2	7	3.2 | 46
Size 0 (Only MidiCaps® & Gamma MidiCaps®)	0.45 m^2 | 4.8 ft^2	14	3.2 | 46
Capsules | Gamma Capsules			
Size 4	0.015 m^2 | 0.16 ft^2	1	3.2 | 46
Size 5	0.03 m^2 | 0.32 ft^2	2	3.2 | 46

Max. Allowable Differential Pressure

Mini Cartridges \| Cartridges
5 bar \| 72.5 psi at 20°C
2 bar \| 29 psi at 80°C

T-Style MaxiCaps® \| MaxiCaps® \| Gamma MaxiCaps® \| MidiCaps® \| Gamma MidiCaps®
5 bar \| 72.5 psi at 20°C
3 bar \| 43.5 psi at 50°C

Capsules \| Gamma Capsules
4 bar \| 58 psi at 20°C
2 bar \| 29 psi at 50°C

Max. Allowable Back Pressure

2 bar \| 29 psi at 20°C
(for all elements)

Materials

Prefilter Membrane
Polyethersulfone, asymmetric

Endfilter Membrane
Polyethersulfone, asymmetric

Support Fleece
Polypropylene
(In-Line Steam sterilizable & autoclavable)
Polyester
(γ-irradiatable or γ-irradiatable \| autoclavable)

Core
Polypropylene

End Caps
Polypropylene

Capsule Housing
Polypropylene

O-Ring
Silicone
(other materials on request)

Filling Bell
Polycarbonate

Pore Size Combination

0.45 µm + 0.2 µm

Regulatory Compliance

- Each individual element is tested for integrity by Bubble Point and Diffusion test
- Fully validated as sterilizing grade filters according to ASTM current F-838 guidelines
- Designed, developed and manufactured in accordance with an ISO 9001 certified Quality Management System
- Meet or exceed the requirements for WFI quality standards set by the current USP
- Non pyrogenic according to USP Bacterial Endotoxins
- USP Plastic Class VI Test
- Non fiber releasing according to 21 CFR

Sterilization

Mini Cartridges, Cartridges

In-Line Steam Sterilization
134 °C, 0.3 bar, 20 min.
Min. 25 Sterilization Cycles

or

Autoclaving
134°C, 2 bar, 30 min
Min. 25 Sterilization Cycles

MaxiCaps®, MidiCaps® & Capsules

Autoclaving
134°C, 2 bar, 30 min
Min. 25 Sterilization Cycles (MidiCaps® & MaxiCaps®)
Min. 5 Sterilization Cycles (Capsules)

Gamma MaxiCaps®, Gamma MidiCaps® & Gamma Capsules

Gamma Irradiation
≤ 50 kGy
1 Sterilization Cycle

T-Style MaxiCaps®

Autoclaving
134°C, 2 bar, 30 min
Min. 5 Sterilization Cycles

or

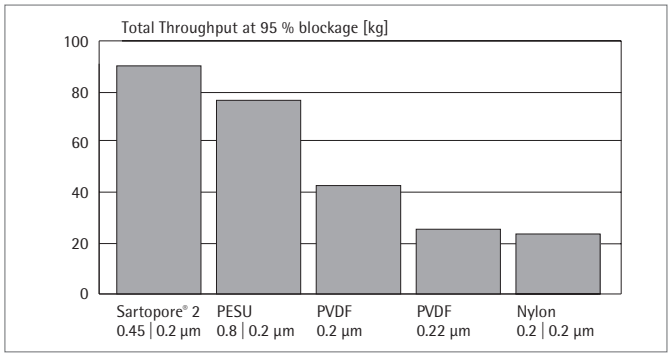
Gamma Irradiation
≤ 50 kGy
1 Sterilization Cycle

Technical References

Validation Guide	SPK5802-e
Extractables Guide	SPK5731-e

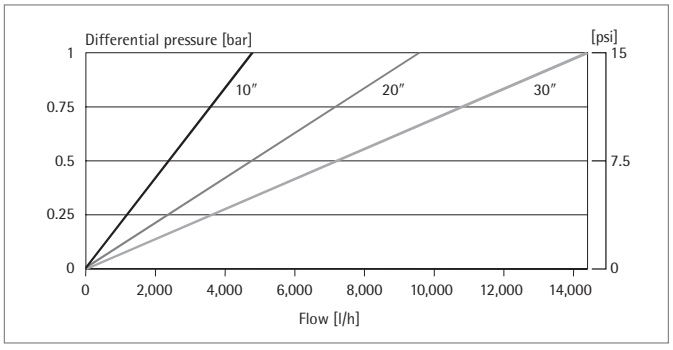
Performance

Total Throughput Comparison



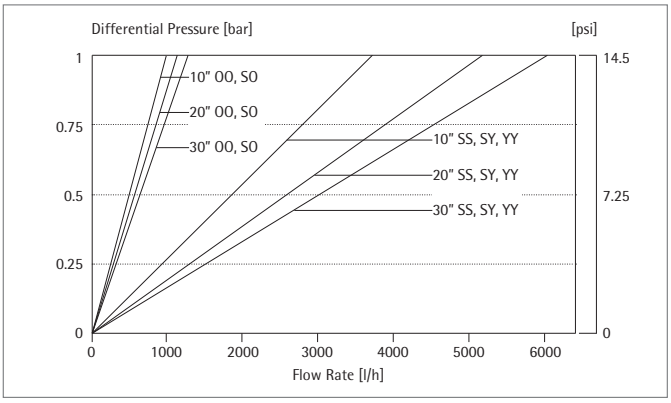
10″ Cartridge format

Water Flow Rates for Standard Cartridges



Standardized at 20 °C

Water Flow Rates for T-Style MaxiCaps®



Ordering Information

Mini Cartridge

544	15	07	H	•	--	-	-	--	--	B

Adapter
15: Bayonet adapter with o-ring
18: Plug Adapter with double o-ring

Filter Size
7: 0.05 m^2 | 0.5 ft^2
8: 0.1 m^2 | 1.1 ft^2
9: 0.2 m^2 | 2.2 ft^2

Packing Size
B: box of 5

(Standard with silicone o-ring optional with EPDM o-ring. Example: 5441507H7---E--B)

Cartridge

544	25	07	H	•

Adapter
21: double open end with flat gaskets
25: 2 Flange Bayonet adapter with 226 double o-ring
27: Bayonet adapter with 222 double o-ring
28: 3 Flange Bayonet adapter with 222 double o-ring

Filter Size
0: 0.3 m^2 | 3.2 ft^2 (5")
1: 0.6 m^2 | 6.5 ft^2 (10")
2: 1.2 m^2 | 12.9 ft^2 (20")
3: 1.8 m^2 | 19.4 ft^2 (30")

(Standard with silicone o-ring optional with EPDM o-ring. Example: 5442507H1---E)

T-Style MaxiCaps®

544	83	07	H	•	G-	•	•

Filter Size
1: 0.6 m^2 | 6.5 ft^2 (10")
2: 1.2 m^2 | 12.9 ft^2 (20")
3: 1.8 m^2 | 19.4 ft^2 (30")

Sterilization
G-: γ-irradiatable and autoclavable

Connector Inlet
S: 1½" Tri-Clamp 50 mm
O: ½" single stepped hose barb
Y: 1" single stepped hose barb

Connector Outlet
S: 1½" Tri-Clamp 50 mm
O: ½" single stepped hose barb
Y: 1" single stepped hose barb

MaxiCaps® | Gamma MaxiCaps®

544	73	07	H	•	•	•	•

Filter Size
1: 0.6 m^2 | 6.5 ft^2 (10")
2: 1.2 m^2 | 12.9 ft^2 (20")
3: 1.8 m^2 | 19.4 ft^2 (30")

Sterilization
G-: γ-irradiatable
--: autoclavable

Connector Inlet
S: 1½" Tri-Clamp 50 mm
O: ½" single stepped hose barb
F: ¾" Tri-Clamp 25 mm

Connector Outlet
S: 1½" Tri-Clamp 50 mm
O: ½" single stepped hose barb
F: ¾" Tri-Clamp 25 mm

(Optional with vent valve design for connection of integrity tester. Example: 5447307H1--SSIT)

MidiCaps® | Gamma MidiCaps®

544	53	07	H	•	•	•	•	--	•

Filter Size
7: 0.05 m^2 | 0.5 ft^2
8: 0.1 m^2 | 1.1 ft^2
9: 0.2 m^2 | 2.2 ft^2
0: 0.45 m^2 | 4.8 ft^2

Sterilization
G-: γ-irradiatable
--: autoclavable

Connector Inlet
S: 1½" Tri-Clamp 50 mm
O: ½" single stepped hose barb
F: ¾" Tri-Clamp 25 mm
H: ¼" multiple stepped hose barb (only size 7 with filling bell)

Connector Outlet
S: 1½" Tri-Clamp 50 mm
O: ½" single stepped hose barb
F: ¾" Tri-Clamp 25 mm
H: ¼" multiple stepped hose barb (only size 7 with filling bell)

Packing Size
A: box of 4 (size 7,8,9)
V: box of 2 (size 0)

Capsules | Gamma Capsules

544	13	07	H	•	•	•	•	--	B

Filter Size
4: 0.015 m^2 | 0.16 ft^2
5: 0.03 m^2 | 0.32 ft^2

Sterilization
G-: γ-irradiatable
--: autoclavable

Connector Inlet
S: ¾" Tri-Clamp 25 mm
O: ¼" multiple stepped hose barb

Connector Outlet
S: ¾" Tri-Clamp 25 mm
O: ¼" multiple stepped hose barb

Packing Size
B: box of 5

Check the availability of your desired configuration with your Sartorius sales representative or online at:

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POROS™ HIC Resins: Ethyl, Benzyl, and Benzyl Ultra

Pub. No. 100063752 **Rev.** A

WARNING! Read the Safety Data Sheets (SDSs) and follow the handling instructions. Wear appropriate protective eyewear, clothing, and gloves. Safety Data Sheets (SDSs) are available from **thermofisher.com/support**.

Product information

Product description

POROS™ Hydrophobic Interaction Chromatography (HIC) resins are rigid, 50-µL polymeric resins with a range of hydrophobic functionalities for the purification of antibody fragments, antibody drug conjugates (ADCs), recombinant proteins, viruses, and other biomolecules. The resin backbone consists of crosslinked poly(styrene-divinylbenzene) with a unique pore structure that provides rapid mass transport and enables enhanced productivity. The particle surface is coated with a novel polymer coating, which is then further derivatized with a range of hydrophobic ligands for flexible purification process design.

POROS™ HIC resins are suitable for bind/elute and flow-through applications at lower salt concentrations. These resins have superior resolution capability, high capacity, and differentiating selectivity for a range of biomolecules, and this performance is independent of flow rate.

Storage

Store resins at 2– 30°C. Do not freeze.

Specifications

Table 1 Ligands, hydrophobicity, and applications

Resin	Ligand	Relative hydrophobicity [1]	Application
Ethyl	Novel ethyl	Low	Bind/elute mode to bind moderately to strongly hydrophobic molecules.
Benzyl	Low-density benzyl/ aromatic	Moderate	Bind/elute or flow-through mode depending on the hydrophobicity of the molecule.
Benzyl Ultra	High-density benzyl/ aromatic	High	Flow-through mode in lower salt concentration to bind impurities such as aggregates.

[1] Hydrophobicity results are based on lysozyme gradient elution. Column size: 0.66 cmD × 20 cmL; 1.7-M ammonium sulfate, 50-mM sodium phosphate pH 7.0; Gradient elution: 1.7-M ammonium sulfate/50 mM sodium phosphate pH 7.0 to 50-mM sodium phosphate pH 7.0 over 10 column volumes; Flow rate: 100 cm/hr.

Table 2 Characteristics and stability

Characteristic	Description
Support matrix	Crosslinked poly(styrene-divinylbenzene)
Shipping solution	18% ethanol
Average particle size	50 µm
Mechanical resistance	100 bar (1450 psi, 10 MPa)
pH range	1–14
Ionic strength range	0 to 5 M, all common salts
Buffer additives	All common agents, including 1 M sodium hydroxide, 8 M urea, 6 M guanidine hydrochloride, ethylene glycol, and detergents
Salts	Ammonium sulfate, sodium sulfate, sodium chloride, sodium acetate, sodium citrate and other common salts **IMPORTANT!** POROS™ Benzyl and POROS™ Benzyl Ultra are designed for use with lower salt concentration than traditional HIC resins. With some molecules, high salt concentration can cause poor recovery due to a strong interaction between the target and the ligand.
Solvents	Water, 0–100% alcohol, acetonitrile, 1 to 2 M acids (for example, acetic, hydrochloric, phosphoric), other common organic solvents Do not expose to strong oxidizers (such as hypochlorite), oxidizing acids (such as nitric), strong reducing agents (such as sulfite), acetone, or benzyl alcohol.
Shrinkage/swelling	<1% from 1–100% solvent
Operating temperature	2– 30°C Do not freeze

POROS™ HIC resins can be operated at high linear flow rates with a pressure drop that allows use with conventional low-pressure chromatography columns and systems. POROS™ HIC resins have linear and predictable pressure flow responses as column diameter increases (Figure 1 and Figure 2).

Product usage: See "Ordering information" on page 5.

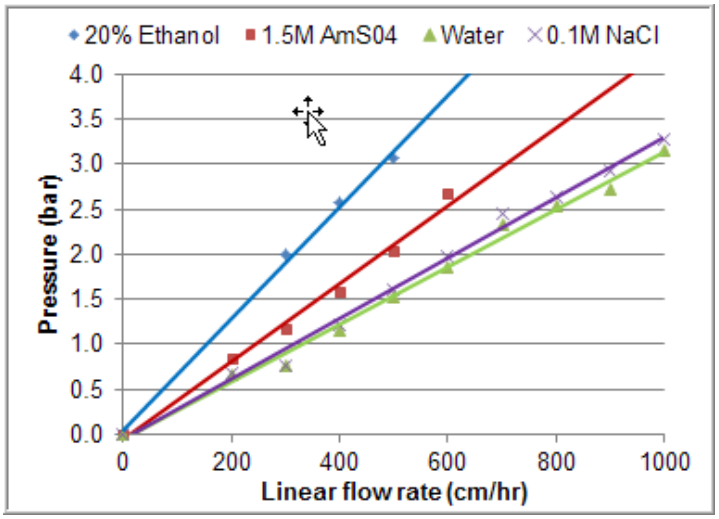

Fig. 1 Pressure-flow properties of POROS™ Ethyl resin—20-cm bed height

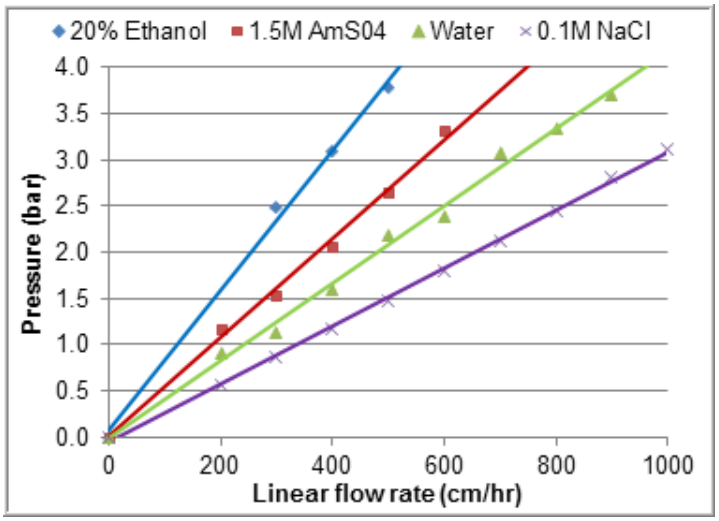

Fig. 2 Pressure-flow properties of POROS™ Benzyl Ultra resin—20-cm bed height

Pack and qualify the column

Packing guidelines

- Resins are supplied in 18% ethanol. For column packing, exchange the shipping solution with water to remove the ethanol.
- Resins are mechanically rigid and incompressible and can be packed effectively in low-pressure glass columns and in high-pressure stainless steel columns. The lack of wall support with increasing column diameter has minimal impact on chromatography performance because the beads support themselves, allowing for flexible column packing approaches and consistent and robust results. Columns can be packed with traditional flow pack, axial compression, or pack-in-place/stall pack packing methods.
- Standard 10–23 µm screens (frits) can be used.

Prepare slurry: lab-scale columns (≤ 100 mL)

Buffer-exchange using a 0.2–0.45 µm bottle-top filter or sintered-glass filter:

1. Transfer the required volume of resin slurry to the top of a bottle-top filter.
2. Apply vacuum to remove the shipping solution.
3. Resuspend the resin cake to the starting resin slurry volume with water. Mix with a plastic or rubber spatula. Do not grind the resin bed or tear the filter membrane.
4. Repeat the vacuum and resuspension steps for a total of three exchanges.
5. Resuspend the exchanged resin to the original slurry concentration, then proceed with column packing.
6. Verify that the slurry concentration is 50–70% (see "Determine the slurry concentration" on page 2).
7. If needed, adjust the slurry concentration to 50–70%.

Prepare slurry: lab-scale and larger scale columns (> 100 mL)

Buffer-exchange using repeated gravity settling:

1. Allow the resin to settle in the shipping container. Settling requires > 8 hours because the density of the resin is approximately that of water.
2. Carefully decant the supernatant. Do not disturb the bed.

   Some particles/turbidity may be present in the decant as beads slough off the settled bed or come loose from the carboy side walls. This is not problematic.
3. Replace the supernatant with the same volume of the desired packing solution.
4. Replace the supernatant with the same volume of water.
5. Resuspend the resin by gentle agitation, then allow the resin to settle by gravity.
6. Repeat steps 1 to 4 two to three times to thoroughly exchange into water.
7. Verify that the slurry concentration is 50–70% (see "Determine the slurry concentration" on page 2).
8. If needed, adjust the slurry concentration to 50–70%.

Determine the slurry concentration

1. Separate the slurry using either of the following methods.
   - **Gravity settling**—Add 100 mL of slurry in water to a 100-mL graduated cylinder, then allow to settle for >72 hours.

     Note: The time that POROS™ HIC resins take to gravity settle can be inconsistent due to hydrophobicity. We recommend using the centrifugation method for faster, more consistent results.
   - **Centrifugation**—Add 10 mL of slurry in water to three (3) 15-mL conical tubes. Centrifuge at 3,000 rpm for 10 minutes at 20°C with the brake off. Remove the tubes from the centrifuge and allow the tubes to sit for 5 minutes before determining the concentration.
2. Calculate the concentration: Volume of resin/total volume in the graduated cylinder or conical tube.

Pack the column

When you adjust the flow rate to form the bed, you may observe some turbidity in the eluent as packing starts. Turbidity will clear as packing proceeds and 1–2 bed volumes of packing buffer pass through the column.

1. Determine the required slurry volume:

   Example for a POROS™ Ethyl 40 cmD × 20 cmL 25-L column using slurry with a 50% slurry ratio:

   25 L / 0.56 × 1.06 = 47.3 L slurry required

   The 1.06 packing factor above accounts for the difference in bed volume between a centrifuged bed in water and a 3-bar pressure-packed bed. Use a 1.12 packing factor for POROS™ Benzyl and POROS™ Benzyl Ultra.
2. Ensure that the column outlet is closed and plumbed directly to waste. Do not connect the column outlet to the chromatography system. Plumbing into the system creates backpressure that fights against the inlet pressure trying to settle the bed and pack the column.
3. Ensure that the column is level and locked in place before starting the pack.
4. Deliver the required slurry volume to the column by hand or with a diaphragm pump, as dictated by your equipment and the intended packing procedure. Use a squirt bottle containing packing solution to remove any residual resin from the column wall.

   POROS™ resin beads have a skeletal density similar to the density of water and do not settle rapidly. Do not allow the resin to gravity-settle in the column before packing.
5. With the column inlet line connected to the system and the bottom outlet closed, bring the primed top flow adapter to 1–2 cm from the slurry level, then tighten the O-ring. Do not push up the resin and over the O-ring. Change the top valve to force the air and liquid out the top of the adapter and to waste using the bypass line. Continue to lower the adapter slowly to remove the bubbles from the top of the column. Do not allow large air bubbles between the top adaptor and the top of the resin slurry.
6. Change the valve back to flow through the system on the top, then open the column bottom.
7. Increase the flow rate to the maximum or desired flow rate and pressure obtainable with the equipment used.
8. After the bed is formed, bring the adapter into contact with the top of the bed without pushing the resin over the O-ring by closing the column outlet and displacing liquid through the top of the adapter to waste through the bypass line.

   POROS™ resin does not shrink or swell, so an open headspace is not recommended.
9. Flow at the packing flow rate again for 1–2 CVs, taking note of the bed height at the desired pressure. Adjust the adapter again to the noted bed height by displacing the liquid through the top of the adapter and to waste.
10. After the column is packed, flow 2–3 CVs of packing solution through the packed bed at the operating flow rate to stabilize the bed.

    The flow rate used should generate no more than 80% of the final packing pressure.
11. If you will reverse the flow of the column during operation, condition the column in upflow:
    - Flow 2–3 CVs in upflow at the operating flow rate.
    - Flow 2–3 CVs in downflow at the operating flow rate, then adjust the adapter if needed.
    - Flow 2 CVs after you adjust the adapter.

Qualify the column

To qualify the integrity of a packed column, determine HETP (height equivalent to a theoretical plate) and asymmetry using a non-binding analyte (a "plug").

Recommended column qualification conditions

Condition	Recommendation
Flow rate	50 cm/hour
Equilibration buffer	Water
Plug solution	0.5 M sodium chloride
Plug volume	1% of column volume

Guidelines for qualification

- Ensure uniform column plumbing:
  - Avoid using reducers to connect different tubing sizes.
  - Minimize and keep consistent the column tubing lengths between the plug solution to the column inlet and the column outlet to the detector(s).
- Equilibrate with at least 4 CVs of equilibration buffer before injection.

Setting specifications

Qualification results depend on several factors, including the:

- Solutions and method used
- Scale
- Column hardware
- Chromatography system

After you define a column qualification procedure for a specific system (column plus chromatography system), base the qualification acceptance criteria on historical values and ranges instead of theoretical qualification results. Performing the column qualification method consistently and reproducibly is critical to obtaining meaningful results.

Chromatography condition optimization

General guidelines

Standardized conditions or platform-type evaluations are not recommended. Different HIC resins that are operated with the same process conditions can yield variable results.

When optimizing conditions:

- Test different loading and elution conditions to evaluate static binding capacity and yield based on the target molecule characteristics and process challenges.
- Limit static binding load incubation time to 15 minutes.
- Optimize the chromatography step for peak separation: Use conditions that remove some of the bound impurities during the flow-through/wash phase and that retain other bound impurities until elution during the strip and cleaning-in-place (CIP) steps.
- Use buffer salts and reagents of the highest purity.
- Filter (0.22 or 0.45 µm) all buffers, solutions, and load before use.

Resin selection guidelines

- If the hydrophobicity of the target molecule is unknown:
  - Run a small-scale bind/elute gradient separation on POROS™ Benzyl resin to determine the elution conductivity of the target molecule, contaminants, and impurities.
  - Optimize conditions on POROS™ Benzyl Ultra resin (higher hydrophobicity) or POROS™ Ethyl resin (lower hydrophobicity).
  - If needed, continue to optimize conditions on POROS™ Benzyl resin (mid-range hydrophobicity).
- If the target molecule is hydrophobic, optimize conditions on POROS™ Ethyl resin or on POROS™ Benzyl with lower salt concentration.
- For flow-through applications where the target molecule is less hydrophobic, optimize conditions on POROS™ Benzyl or POROS™ Benzyl Ultra with lower salt concentration.

After you select the resin, continue to optimize other process conditions.

Binding capacity and loading condition screening guidelines

Perform high-throughput static binding capacity testing in spin columns or in a 96-well plate to screen POROS™ HIC resin. Optimize loading conditions as needed.

Note: A 96-well high-throughput protocol is available on request. This protocol can be used to evaluate static binding capacity and to screen several resins and loading conditions per resin in a single 96-well plate.

Bind/elute chromatography optimization guidelines

Binding conditions guidelines

- **Salt and salt concentration** — POROS™ HIC resins are designed to use less lyotropic salts and to bind at lower concentrations than traditional HIC resins with similar functional groups (Table 3).

  Table 3 Typical salts used in hydrophobic interaction chromatography in order of decreasing lyotropic ("salting out") effect and increasing chaotropic ("salting in") effect

Effect	Anionic salts	Cationic salts
Most lyotropic	$C_6H_5O_7^{3-}$	NH_4^+
	PO_4^{3-}	Rb^+
	SO_4^{2-}	K^+
	$CH3COO^-$	Na^+
	Cl^-	Cs^+
	Br^-	Li^+
	NO_3^-	Mg^{2+}
	ClO_4^-	Ca^{2+}
Most chaotropic	I^-	Ba^{2+}

  Note the following:
  - You can perform initial binding experiments with lower salt concentrations than are typically used for HIC chromatography. For example, you can start with 25%, 50% and 75% of the salting out concentration, instead of the typical 10–15% lower than the salting out concentration.
  - The optimized ionic salt concentration for the salts listed above can differ from ammonium sulfate, which has been traditionally used for HIC chromatography.
  - Different salts can provide different selectivity.

  Optimize the salt concentration for the target molecule by using a "salting out" experiment: increase the ionic strength of the loading buffer until the sample precipitates. Alternatively, you can measure increasing optical density of the loading buffer to detect aggregation (~350 nm, but this value may differ with each salt). Salts that are commonly used to perform salting out experiments are ammonium sulfate, sodium chloride, sodium citrate, sodium sulfate, and sodium acetate.
- **Buffer system**—Buffer systems are not as critical for HIC processes as they are for ion-exchange chromatography steps. Citrate, acetate, Bis-Tris propane, HEPES, MES, sodium phosphate, succinate, and Tris are commonly used.

  The buffer system is typically dictated by the upstream purification step. When selecting the upstream buffer system, consider molecule stability in the buffer, binding optimization, and buffering capacity.
- **pH**—pH is not typically critical for HIC processes, but it can affect the binding strength and selectivity. Because pH effects are unpredictable on HIC, test a few pH values over the stability range of the target molecule.
- **Flow rate**—The target operating flow rate is flexible. Start optimization at 4-minute residence time (300 cm/hr in a 20-cmL column).
- **Temperature**—Temperature can significantly impact HIC performance. Perform all optimization at the final intended process temperature.

Elution conditions guidelines

Start elution optimization with a gradient elution. Most often, after elution performance is determined, you can implement a step elution.

- **Salt gradient**—To determine where the target molecule and contaminants/ impurities elute, start with a 20-CV gradient from high salt to buffer only. To do so, assay fractions across the peaks (~1/10 CV). Based on this information, the process can be further optimized.
- **Dynamic binding capacity (DBC)**—Assess separation as a function of DBC. The maximum DBC depends on several factors, including sample solubility, column selectivity, buffer pH, and loading buffer conductivity.
- **Bed height**—Initial screening can be run with shorter bed heights and a constant residence time. Use the final desired bed height for scale up development (typically 15 cm to 30 cm).

Flow-through chromatography optimization guidelines

An optional flow-through step can be used remove trace product and process-related impurities such as aggregates from the target molecule. You can add the flow-through step as the second or third chromatography step for polishing in a downstream process. Different target molecules have different degrees of hydrophobicity and other biophysical characteristics. Therefore, it is essential to optimize the process conditions to achieve the desired aggregate clearance and recovery of the target molecule.

Loading conditions guidelines

- **Initial study** —Perform an initial study using a decreasing salt gradient in bind/elute mode:
  - Load approximately 1 mg of protein per 1 ml of resin at 0.5–1.0 M sodium chloride (or other preferred salt), then elute using a gradient over 10 column volumes (CVs) in a buffered solution to determine aggregates, impurities, and target molecule elution profiles.
  - Use the elution conductivity at peak maximum to determine the highest approximate salt concentration that is required to remove impurities, but that allows the target molecule to flow through (Figure 3).

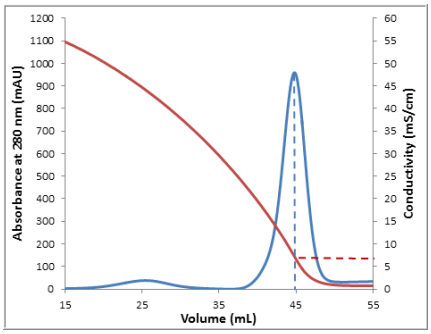

Fig. 3 Example screening chromatogram to obtain the ideal low salt condition for flow-through conditions. Process screening for a monoclonal antibody using POROS™ Benzyl Ultra resin in flow-through mode. Gradient: High conductivity to low conductivity using sodium citrate. Based on this chromatogram, the resin was further optimized in flow-through mode at low salt conditions starting at 7 mS/cm.

- **Buffer system**—Buffer systems are not as critical for HIC processes as they are for ion-exchange chromatography steps. Citrate, acetate, Bis-Tris propane, HEPES, MES, sodium phosphate, succinate, and Tris are commonly used.

  The buffer system is typically dictated by the upstream purification step. When selecting the upstream buffer system, consider molecule stability in the buffer, binding optimization, and buffering capacity.
- **pH**—pH is not typically critical for HIC processes, but it can affect the binding strength and selectivity. Because pH effects are unpredictable on HIC, test a few pH values over the stability range of the target molecule.
- **Flow rate**—The target operating flow rate is flexible. Good impurity binding has been demonstrated at flow rates up to 600 cm/hour on a 20 cmL column (1.6-minute residence time).
- **Temperature**—Temperature can significantly impact HIC performance. Perform all optimization at the final intended process temperature.
- **Dynamic binding capacity (DBC)**—A conservative starting point for DBC determination is 100–250 mg of the target molecule per mL of resin. Determine the DBC for each impurity by using breakthrough analysis under the desired load pH and conductivity conditions.
- **Bed height**—A bed height of 15 cm to 30 cm can be used for this step.

Resin cleaning and storage

Resin cleaning guidelines

- POROS™ resins can tolerate harsh cleaning conditions that allow acceptable column life.
- Clean the resin with 3 to 5 CVs of water followed by 3 to 5 CVs of 1 M NaOH.
- For more stringent cleaning, use 20% ethanol/1 M acetic acid.
- Other solutions may be required for column cleaning if the resin is used for capture chromatography.
- Degas more viscous solutions such as 1 M acetic acid or 20% ethanol before use on the column to avoid gassing out during operation.

  Note: Low-level gassing out does not impact column performance.

Store the resin

Store the resin in 20% ethanol or 0.1 M NaOH at 2–30°C.

Ordering information

Table 4 POROS™ HIC bulk resins

Resin	Cat. No.	Amount	Product usage
Ethyl	A32552	10,000 mL	Pharmaceutical Grade Reagent. For Manufacturing and Laboratory Use Only.
	A32553	5,000 mL	
	A32554	1,000 mL	
	A32555	250 mL	For Research Use Only. Not for use in diagnostic procedures.
	A32556	50 mL	
	A32557	25 mL	
Benzyl	A32558	10,000 mL	Pharmaceutical Grade Reagent. For Manufacturing and Laboratory Use Only.
	A32559	5,000 mL	
	A32560	1,000 mL	
	A32561	250 mL	For Research Use Only. Not for use in diagnostic procedures.
	A32562	50 mL	
	A32563	25 mL	
Benzyl Ultra	A32564	10,000 mL	Pharmaceutical Grade Reagent. For Manufacturing and Laboratory Use Only.
	A32565	5,000 mL	
	A32566	1,000 mL	
	A32567	250 mL	For Research Use Only. Not for use in diagnostic procedures.
	A32568	50 mL	
	A32569	25 mL	

Support

For service and technical support, go to **thermofisher.com/poros** or call toll-free in US: 1.800.831.6844.

For the latest service and support information at all locations, or to obtain Certificates of Analysis or Safety Data Sheets (SDSs; also known as MSDSs), go to **thermofisher.com/support**, or contact you local Thermo Fisher Scientific representative.

Limited product warranty

Life Technologies Corporation and/or its affiliate(s) warrant their products as set forth in the Life Technologies' General Terms and Conditions of Sale found on Life Technologies' website at **www.thermofisher.com/us/en/home/global/terms-and-conditions.html**. If you have any questions, please contact Life Technologies at **www.thermofisher.com/support**.

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Manufacturer: Life Technologies Corporation | 35 Wiggins Avenue | Bedford, MA 01730

The information in this guide is subject to change without notice.

Revision history: Pub. No. 100063752

Revision	Date	Description
A	10 July 2017	New document.

Virosart® CPV MaxiCaps® and Cartridges

The virus filter for the robust and efficient removal of all viruses

Product Information

Virosart® CPV is a well established virus retentive filter within the monoclonal antibody market. The unique assymmetric PES membrane structure provides highest virus retention under all circumstances independent from operation pressure or pressure pauses.

Description

Virus filtration with Virosart® is an integral part of the orthogonal virus clearance technology platform of Sartorius Stedim Biotech. This orthogonal technology platform features virus filtration, virus inactivation and virus adsorption. The Virosart® product ranges includes three different virus retentive membranes, in order to provide the best solution for every application.

Virosart® CPV targets the removal of both small non-enveloped viruses (20 nm) e.g. PPV, MVM and larger enveloped viruses (> 50 nm) e.g. MuLV from a biopharmaceutical feed stream.

Application & Positioning of Virosart® CPV

The main applications for Virosart® CPV for virus filtration are monoclonal antibodies (Mab), antibody fragments (Fab) or small recombinant proteins (<150kD). Virosart® CPV is used at the end of the purification process for virus filtration of the biopharmaceutical product. At this stage the purity of the biopharmaceutical product is the highest and virus filter blockage due to contaminants (DNA, CHOP, aggregates & lipoproteins) is the lowest.

Even if these contaminants should be removed during the polishing process of the target molecule, small amounts might be sufficient to cause premature blockage of the final virus filter. To prevent this, an efficient pre-filtration step, such as the Virosart® Max, might be required as protection for the Virosart® CPV membrane. The optimum pre-filter-final filter ratio has to be identified during development of the process step.

Product Benefits

Virosart® CPV provides highest virus safety to the biopharmaceutical product. Based on the unique double layer 20 nm PES membrane, Virosart® CPV provides excellent flow rates and superior capacity. This filter retains more than 4 $\log^{10}$ of small non-enveloped viruses (e.g. PPV, MVM) and more than 6 $\log^{10}$ of large enveloped viruses (e.g. MuLV). This filter offers highest virus safety over the entire flow decay profile independent of operating pressure or pressure pauses.

Scalability

Scale down work is realised using the Virosart® CPV Minisart (5 cm^2 capsule) to enable filtration work for flow and capacity studies as well as for optimizing the final pre-filter-final filter ration. These elements, available as IT tested devices are also used for reliable scale-down work within GLP virus spiking studies. Scale up studies as well as small scale production are performed using Virosart® CPV capsule and|or MidiCaps® (180 cm^2 | 2.000 cm^2) to reliably scale up into larger scale manufacturing. Large scale manufacturing is operated with Virosart® CPV MaxiCaps® or cartridges. Typical batch sizes of products subject to virus filtration with Virosart® CPV MaxiCaps® and cartridges are ≥ 50 liter.

Integrity Testing
Virosart® CPV filters are tested for integrity using a water based integrity test, e.g. based on the Sartocheck® technology of Sartorius Stedim Biotech. Virosart® CPV filters have been validated for 4 log^{10} removal of small non-enveloped viruses using bacteriophage PP7 as the model virus. Validation data is shown in the validation guide of Virosart® CPV.

Quality Control
Each individual Virosart® CPV filter is autoclaved and integrity tested during manufacture assuring highest product reliability.

Documentation
Virosart® CPV filters are designed, developed and manufactured in accordance with a ISO 9001 certified Quality Management System. A Validation Guide is available for compliance with regulatory requirements.

Technical Data

Specifications

Materials	
Membrane	Double layer polyethersulfone
Support Fleece	Polypropylene
Core	Polypropylene
End Caps	Polypropylene
Capsule Housing	Polypropylene

Pore Size
CPV (20 nm nominal)

Available Sizes | Filtration Area

MaxiCaps®	
Size 1	0.7 m^2 | 7 ft^2
Size 2	1.4 m^2 | 14 ft^2
Size 3	2.1 m^2 | 21 ft^2

Standard Filter Cartridges	
Size 1	0.7 m^2 | 7 ft^2
Size 2	1.4 m^2 | 14 ft^2
Size 3	2.1 m^2 | 21 ft^2

Available Connectors
Sanitary for MaxiCaps® & code 7 for cartridges

Operating Parameters	
In the direction of filtration	At 20°C max. 5.0 bar | 72.5 psi At 121°C max. 0.2 bar | 2.9 psi
In the reversed direction of filtration	At 20°C max. 0.2 bar | 2.9 psi

Extractables
Virosart® CPV filters meet, or exceed the requirements for WFI quality standards set by the USP 26

Non-pyrogenic according to USP Bacterial Endotoxins

Passes USP Plastics Class VI Test

Non-fiber releasing according to 21 CFR

Sterilization
Steaming (Virosart® CPV cartridges only!):
121°C @ 1 bar | 14.5 psi for 30 min
up to 2 cycles

Autoclaving:
121°C @ 1 bar | 14.5 psi for 30 min
up to 2 cycles

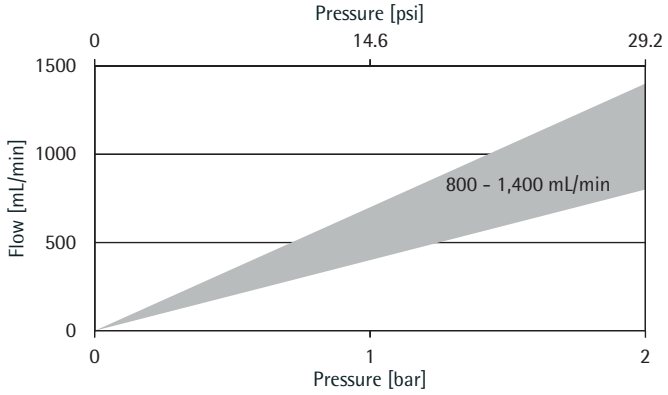
No In-Line Steam Sterilization of MaxiCaps®!

Technical References
Validation Guide: SPK5754-e | 85030-522-02

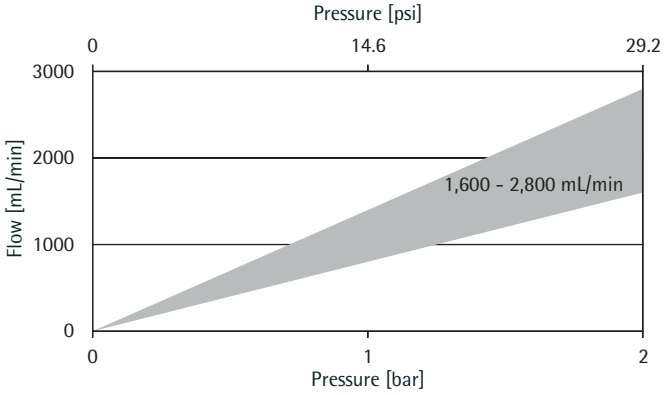
Extractable Guide: SPK5773-e | 85034-536-47

Virus Information Guide: SPK5752-e | 85030-521-91

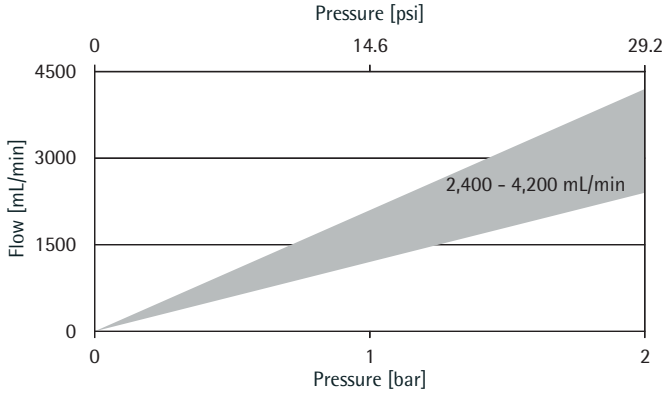
Characteristic Water Flow Rates for Virosart® CPV 10" Standard Filter Cartridges & 10" MaxiCaps®



Characteristic Water Flow Rates for Virosart® CPV 20" Standard Filter Cartridges & 20" MaxiCaps®



Characteristic Water Flow Rates for Virosart® CPV 30" Standard Filter Cartridges & 30" MaxiCaps®



Ordering Information

Ordering Information Virosart® CPV Standard Filter Cartridges

545	25	28	V1	Explanation
				Virosart® CPV, double layer
	25			**Adapter** **25**: S-adapter top, locking bayonet adapter with double O-ring bottom
		28		**Pore Size** **28**: PPV retentive, 20 nm filter membrane
			V1	**Height Filtration Area** **V1**: 10" 0.7 m² | 7 ft² **V2**: 20" 1.4 m² | 14 ft² **V3**: 30" 2.1 m² | 21 ft²

Ordering Information Virosart® CPV MaxiCaps®

545	73	28	V1	--	SS	Explanation
						Virosart® CPV, double layer
	73					**Capsule Design** **13**: Old MaxiCaps® design **73**: New MaxiCaps® desgin
		28				**Pore Size** **28**: PPV retentive, 20 nm filter membrane
			V1			**Height Filtration Area** **V1**: 10" 0.7 m² | 7 ft² **V2**: 20" 1.4 m² | 14 ft² **V3**: 30" 2.1 m² | 21 ft²
					SS	**Adapter** **SS** Sanitary inlet – and outlet adapter

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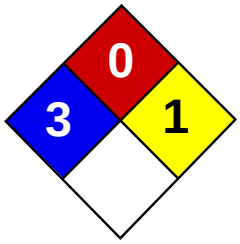

Material Safety Data Sheet

Sodium hydroxide, Pellets, Reagent ACS MSDS

Section 1: Chemical Product and Company Identification

Product Name: Sodium hydroxide, Pellets, Reagent ACS

Catalog Codes: SLS4090

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.
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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: Not available. TERATOGENIC EFFECTS: Not available. DEVELOPMENTAL TOXICITY: Not available. The substance is toxic to lungs. 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: 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 heat.

Fire Fighting Media and Instructions: Not applicable.

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, ally alcohol, allyl chloride, benzene-1,4-diol, chlorine trifluoride, 1,2 dichlorethylene, 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 spontanously 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 aquesous sodium hydroxide, under vacuum distillation, residue darkened and exploded. Sodium Hydroxde + 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. 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:
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:
CEIL: 2 from ACGIH (TLV) [United States] [1995] 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: 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: Not available.

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 tetrahyrofuran is very exothermic, a mild explosion being noted on one occassion. Reactive with water, acids, acid chlorides, strong bases, strong oxidizing agents, strong reducing agents, flammable liquids, organic halogens, metals (i.e aluminum, tin, zinc), nitromethane, glacial acetic acid, acetic anhydride, acrolein, chlorohydrin, chlorosulfonic acid, ethylene cyanohydrin, glyoxal, hydrochloric acid, sulfuric acid, hydrosulfuric acid, nitric acid, oleum, propiolactone, acylonitrile, phorosous 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: Causes damage to the following organs: lungs.

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 (mutagenic). Investigation as a mutagen (cytogenetic analysis), but no data available.

Special Remarks on other Toxic Effects on Humans:
Acute Potential Health Effects: Skin: May be harmful if absorbed through skin. Causes severe skin irritation and burns. May cause deep penetrating ulcers of the skin. Eyes: Causes severe eye irritation and burns. May cause chemical conjunctivitis and corneal damage. Inhalation: Harmful if inhaled. Causes severe irritation of the respiratory tract and mucous membranes with coughing, burns, breathing difficulty, and possible coma. Irritation may lead the chemical pneumonitis and pulmonary edema. Causes chemical burns to the respiratory tract and mucous membranes. Ingestion: May be fatal if swallowed. May cause severe and permanent damage to the digestive tract. Causes severe gastrointestinal tract irritation and burns. May cause perforation of the digestive tract. Causes severe pain, nausea, vomiting, diarrhea, and shock. May cause corrosion and permanent destruction of the esophagus and digestive 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: 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):

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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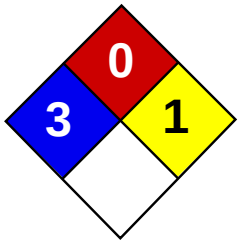

Material Safety Data Sheet
Sodium Hydroxide, 50% MSDS

Section 1: Chemical Product and Company Identification

Product Name: Sodium Hydroxide, 50%

Catalog Codes: SLS3127, SLS4549

CAS#: Mixture.

RTECS: Not applicable.

TSCA: TSCA 8(b) inventory: Sodium hydroxide; Water

CI#: Not applicable.

Synonym: Sodium Hydroxide, 50% Solution

Chemical Name: Not applicable.

Chemical Formula: Not applicable.

Contact Information:

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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	50
Water	7732-18-5	50

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, . 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 is toxic to lungs. 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. Immediately flush eyes with running water for at least 15 minutes, keeping eyelids open. Cold water may be used. Get medical attention immediately. Finish by rinsing thoroughly with running water to avoid a possible infection.

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. Seek 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: 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:
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 aquesous sodium hydroxide, under vacuum distillation, residue darkened and exploded. Sodium Hydroxde + 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. (Sodium hydroxide)

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 acetic acid.

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 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:
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, moisture.

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:
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:
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 NIOSHConsult local authorities for acceptable exposure limits.

Section 9: Physical and Chemical Properties

Physical state and appearance: Liquid.

Odor: Odorless.

Taste: Alkaline. Bitter. (Strong.)

Molecular Weight: Not applicable.

Color: Clear Colorless.

pH (1% soln/water): Basic.

Boiling Point: 140°C (284°F)

Melting Point: 12°C (53.6°F)

Critical Temperature: Not available.

Specific Gravity: 1.53 (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.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Excess heat, incompatible materials, water/moisture

Incompatibility with various substances:
Reactive with oxidizing agents, reducing agents, metals, acids, alkalis. Slightly reactive with water

Corrosivity:
Extremely corrosive in presence of aluminum, brass. Corrosive in presence of copper, of stainless steel(304), of stainless steel(316). Non-corrosive in presence of glass.

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. Generates considerable heat when a sodium hydroxide solution is mixed with an acid Sodium hydroxide solution and octanol + diborane during a work-up of a reaction mixture of oxime and diborane in tetrahyrofuran is very exothermic, a mild explosion being noted on one occassion. 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, foraldehyde), 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. berylium, lead acetate, nickel carbonyl, tetraethyl lead), mitrides (e.g. potassium nitride, sodium nitride), nitriles (e.g. acetonitrile, methyl cyanide), nitro compounds (organic e.g. nitrobenzene, nitromethane), acetic anhydride, hydroquinone, chlorohydrin, chlorosulfonic acid, ethylene cyanohydrin, glyoxal, hydrosulfuric acid, oleum, propiolactone, acylonitrile, phorosous pentoxide, chloroethanol, chloroform-methanol, tetrahydroborate, cyanogen azide, 1,2,4,5 tetrachlorobenzene, cinnamaldehyde. Reacts with formaldehyde hydroxide to yield formic acid, and hydrogen. (Sodium hydroxide)

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.

Toxicity to Animals:
LD50: Not available. LC50: Not available.

Chronic Effects on Humans: Not available.

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: Not available.

Special Remarks on Chronic Effects on Humans: Investigation as a mutagen (cytogenetic analysis), but no data available. (Sodium hydroxide)

Special Remarks on other Toxic Effects on Humans:
Acute Potential Health Effects: Skin: May be harmful if absorbed through skin. Causes severe skin irritation and burns. May cause deep penetrating ulcers of the skin. Eyes: Causes severe eye irritation and burns. May cause chemical conjunctivitis and corneal damage. Inhalation: Harmful if inhaled. Causes severe irritation of the respiratory tract and mucous membranes with coughing, burns, breathing difficulty, and possible coma. Irritation may lead the chemical pneumonitis and pulmonary edema. Causes chemical burns to the respiratory tract and mucous membranes. Ingestion: May be fatal if swallowed. May cause severe and permanent damage to the digestive tract. Causes

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: : Sodium hydroxide, solution (Sodium hydroxide) UNNA: UN1824 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 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):

CLASS D-2A: Material causing other toxic effects (VERY TOXIC). CLASS E: Corrosive liquid.

DSCL (EEC):

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: Not available.

Other Special Considerations: Not available.

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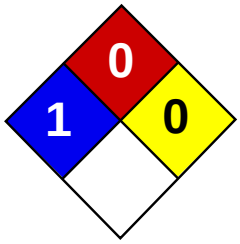

Health	1
Fire	0
Reactivity	0
Personal Protection	E

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:

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International Sales: **1-281-441-4400**

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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 n 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 spasicity/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 Indutrial 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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Nitrogen, refrigerated liquid

Safety Data Sheet P-4630

This SDS conforms to U.S. Code of Federal Regulations 29 CFR 1910.1200, Hazard Communication.

Date of issue: 01/01/1979 Revision date: 10/21/2016 Supersedes: 10/03/2014

SECTION: 1. Product and company identification

1.1. Product identifier

Product form	:	Substance
Name	:	Nitrogen, refrigerated liquid
CAS No	:	7727-37-9
Formula	:	N2
Other means of identification	:	Nitrogen (cryogenic liquid), Nitrogen, Medipure Liquid Nitrogen

1.2. Relevant identified uses of the substance or mixture and uses advised against

Use of the substance/mixture	:	Medical applications Industrial use Food applications

1.3. Details of the supplier of the safety data sheet

Praxair, Inc.
10 Riverview Drive
Danbury, CT 06810-6268 - USA
T 1-800-772-9247 (1-800-PRAXAIR) - F 1-716-879-2146
www.praxair.com

1.4. Emergency telephone number

Emergency number	:	Onsite Emergency: 1-800-645-4633 CHEMTREC, 24hr/day 7days/week — Within USA: 1-800-424-9300, Outside USA: 001-703-527-3887 (collect calls accepted, Contract 17729)

SECTION 2: Hazard identification

2.1. Classification of the substance or mixture

GHS-US classification

Refrigerated liquefied gas H281

2.2. Label elements

GHS-US labeling

Hazard pictograms (GHS-US) :

GHS04

Signal word (GHS-US)	:	WARNING
Hazard statements (GHS-US)	:	H281 - CONTAINS REFRIGERATED GAS; MAY CAUSE CRYOGENIC BURNS OR INJURY OSHA-H01 - MAY DISPLACE OXYGEN AND CAUSE RAPID SUFFOCATION
Precautionary statements (GHS-US)	:	P202 - Do not handle until all safety precautions have been read and understood P271+P403 - Use and store only outdoors or in a well-ventilated place P282 - Wear cold insulating gloves/face shield/eye protection. cold insulating gloves, face shield, eye protection CGA-PG05 - Use a back flow preventive device in the piping CGA-PG24 - DO NOT change or force fit connections CGA-PG06 - Close valve after each use and when empty CGA-PG23 - Always keep container in upright position

2.3. Other hazards

Other hazards not contributing to the	:	Asphyxiant in high concentrations

classification | Contact with liquid may cause cold burns/frostbite.

2.4. Unknown acute toxicity (GHS US)

No data available

SECTION 3: Composition/Information on ingredients

3.1. Substance

Name	Product identifier	%
Nitrogen, refrigerated liquid (Main constituent)	(CAS No) 7727-37-9	100

3.2. Mixture

Not applicable

SECTION 4: First aid measures

4.1. Description of first aid measures

First-aid measures after inhalation : Remove victim to uncontaminated area wearing self contained breathing apparatus. Keep victim warm and rested. Call a doctor. Apply artificial respiration if breathing stopped.

First-aid measures after skin contact : The liquid may cause frostbite. For exposure to liquid, immediately warm frostbite area with warm water not to exceed 105°F (41°C). Water temperature should be tolerable to normal skin. Maintain skin warming for at least 15 minutes or until normal coloring and sensation have returned to the affected area. In case of massive exposure, remove clothing while showering with warm water. Seek medical evaluation and treatment as soon as possible.

First-aid measures after eye contact : Immediately flush eyes thoroughly with water for at least 15 minutes. Hold the eyelids open and away from the eyeballs to ensure that all surfaces are flushed thoroughly. Contact an ophthalmologist immediately.. Get immediate medical attention.

First-aid measures after ingestion : Ingestion is not considered a potential route of exposure.

4.2. Most important symptoms and effects, both acute and delayed

No additional information available

4.3. Indication of any immediate medical attention and special treatment needed

None.

SECTION 5: Firefighting measures

5.1. Extinguishing media

Suitable extinguishing media : Use extinguishing media appropriate for surrounding fire.

5.2. Special hazards arising from the substance or mixture

Reactivity : No reactivity hazard other than the effects described in sub-sections below.

5.3. Advice for firefighters

Firefighting instructions : DANGER! Extremely cold liquid and gas under pressure. Take care not to direct spray onto vents on top of container. Do not discharge sprays directly into liquid; cryogenic liquid can freeze water rapidly

Evacuate all personnel from the danger area. Use self-contained breathing apparatus (SCBA) and protective clothing. Immediately cool containers with water from maximum distance. Stop flow of gas if safe to do so, while continuing cooling water spray. Remove ignition sources if safe to do so. Remove containers from area of fire if safe to do so. On-site fire brigades must comply with OSHA 29 CFR 1910.156 and applicable standards under 29 CFR 1910 Subpart L—Fire Protection.

Protection during firefighting : Compressed gas: asphyxiant. Suffocation hazard by lack of oxygen.

Special protective equipment for fire fighters : Use self-contained breathing apparatus. Standard protective clothing and equipment (Self Contained Breathing Apparatus) for fire fighters.

Specific methods	:	Use fire control measures appropriate for the surrounding fire. Exposure to fire and heat radiation may cause gas containers to rupture. Cool endangered containers with water spray jet from a protected position. Prevent water used in emergency cases from entering sewers and drainage systems Exposure to fire may cause containers to rupture/explode Stop flow of product if safe to do so Use water spray or fog to knock down fire fumes if possible If leaking do not spray water onto container. Water surrounding area (from protected position) to contain fire.
Other information	:	Cryogenic liquid causes severe frostbite, a burn-like injury. Heat of fire can build pressure in a closed container and cause it to rupture. Venting vapors may obscure visibility. Air will condense on surfaces such as vaporizers or piping exposed to liquid or cold gas. Nitrogen, which has a lower boiling point than oxygen, evaporates first, leaving an oxygen-enriched condensate Containers are equipped with a pressure relief device. (Exceptions may exist where authorized by DOT.).

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

General measures	:	Evacuate area. Ensure adequate air ventilation. Wear self-contained breathing apparatus when entering area unless atmosphere is proven to be safe. Prevent from entering sewers, basements and workpits, or any place where its accumulation can be dangerous. Stop leak if safe to do so.

6.1.1. For non-emergency personnel

No additional information available

6.1.2. For emergency responders

No additional information available

6.2. Environmental precautions

Try to stop release.

6.3. Methods and material for containment and cleaning up

No additional information available

6.4. Reference to other sections

See also sections 8 and 13.

SECTION 7: Handling and storage

7.1. Precautions for safe handling

Precautions for safe handling	:	Wear leather safety gloves and safety shoes when handling cylinders. Protect cylinders from physical damage; do not drag, roll, slide or drop. While moving cylinder, always keep in place removable valve cover. Never attempt to lift a cylinder by its cap; the cap is intended solely to protect the valve. When moving cylinders, even for short distances, use a cart (trolley, hand truck, etc.) designed to transport cylinders. Never insert an object (e.g, wrench, screwdriver, pry bar) into cap openings; doing so may damage the valve and cause a leak. Use an adjustable strap wrench to remove over-tight or rusted caps. Slowly open the valve. If the valve is hard to open, discontinue use and contact your supplier. Close the container valve after each use; keep closed even when empty. Never apply flame or localized heat directly to any part of the container. High temperatures may damage the container and could cause the pressure relief device to fail prematurely, venting the container contents. For other precautions in using this product, see section 16.

7.2. Conditions for safe storage, including any incompatibilities

Storage conditions : Store in a cool, well-ventilated place. Store and use with adequate ventilation. Store only where temperature will not exceed 125°F (52°C). Firmly secure containers upright to keep them from falling or being knocked over. Install valve protection cap, if provided, firmly in place by hand. Store full and empty containers separately. Use a first-in, first-out inventory system to prevent storing full containers for long periods

OTHER PRECAUTIONS FOR HANDLING, STORAGE, AND USE: When handling product under pressure, use piping and equipment adequately designed to withstand the pressures to be encountered. Never work on a pressurized system. Use a back flow preventive device in the piping. Gases can cause rapid suffocation because of oxygen deficiency; store and use with adequate ventilation. If a leak occurs, close the container valve and blow down the system in a safe and environmentally correct manner in compliance with all international, federal/national, state/provincial, and local laws; then repair the leak. Never place a container where it may become part of an electrical circuit.

7.3. Specific end use(s)

None.

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Nitrogen, refrigerated liquid (7727-37-9)	
ACGIH	Not established
USA OSHA	Not established

8.2. Exposure controls

Appropriate engineering controls : Oxygen detectors should be used when asphyxiating gases may be released. Systems under pressure should be regularly checked for leakages. Provide adequate general and local exhaust ventilation. Consider work permit system e.g. for maintenance activities.

Hand protection : Wear working gloves when handling gas containers.

Eye protection : Wear safety glasses with side shields. Wear goggles and a face shield when transfilling or breaking transfer connections.

Respiratory protection : Self contained breathing apparatus (SCBA) or positive pressure airline with mask are to be used in oxygen-deficient atmospheres.

Thermal hazard protection : Wear cold insulating gloves. Wear cold insulating gloves when transfilling or breaking transfer connections.

Environmental exposure controls : None necessary.

Other information : Wear safety shoes while handling containers.

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Physical state : Gas

Appearance : Colorless liquid.

Molecular mass : 28 g/mol

Color : Colorless liquid.

Odor : No odor warning properties.

Odor threshold : No data available

pH : Not applicable.

Relative evaporation rate (butyl acetate=1) : No data available

Relative evaporation rate (ether=1) : Not applicable.

Melting point : -210 °C

Freezing point : No data available

Boiling point : -195.8 °C

Flash point : No data available

Critical temperature : -149.9 °C

Auto-ignition temperature	:	Not applicable.
Decomposition temperature	:	No data available
Flammability (solid, gas)	:	No data available
Vapor pressure	:	Not applicable.
Critical pressure	:	3390 kPa
Relative vapor density at 20 °C	:	No data available
Relative density	:	0.8
Density	:	808.5 kg/m³ Liquid density at boiling point and 1 atm
Relative gas density	:	0.97
Solubility	:	Water: 20 mg/l
Log Pow	:	Not applicable.
Log Kow	:	Not applicable.
Viscosity, kinematic	:	Not applicable.
Viscosity, dynamic	:	Not applicable.
Explosive properties	:	Not applicable.
Oxidizing properties	:	None.
Explosion limits	:	No data available

9.2. Other information

Gas group	:	Refrigerated liquefied gas
Additional information	:	Gas/vapor heavier than air. May accumulate in confined spaces, particularly at or below ground level

SECTION 10: Stability and reactivity

10.1. Reactivity

No reactivity hazard other than the effects described in sub-sections below.

10.2. Chemical stability

Stable under normal conditions.

10.3. Possibility of hazardous reactions

None.

10.4. Conditions to avoid

Avoid high temperatures, exposure to Lithium (Li), Neodymium (Nd), Titanium (Ti), Magnesium.

10.5. Incompatible materials

None.

10.6. Hazardous decomposition products

Under certain conditions, nitrogen can react violently with lithium, neodymium, titanium (above 1472°F/800°C), and magnesium to form nitrides. At high temperature, it can also combine with oxygen and hydrogen.

SECTION 11: Toxicological information

11.1. Information on toxicological effects

Acute toxicity	:	Not classified
Skin corrosion/irritation	:	Not classified pH: Not applicable.
Serious eye damage/irritation	:	Not classified pH: Not applicable.
Respiratory or skin sensitization	:	Not classified
Germ cell mutagenicity	:	Not classified
Carcinogenicity	:	Not classified

Reproductive toxicity	:	Not classified
Specific target organ toxicity (single exposure)	:	Not classified
Specific target organ toxicity (repeated exposure)	:	Not classified
Aspiration hazard	:	Not classified

SECTION 12: Ecological information

12.1. Toxicity

Ecology - general : No ecological damage caused by this product.

12.2. Persistence and degradability

Nitrogen, refrigerated liquid (7727-37-9)	
Persistence and degradability	No ecological damage caused by this product.

12.3. Bioaccumulative potential

Nitrogen, refrigerated liquid (7727-37-9)	
Log Pow	Not applicable.
Log Kow	Not applicable.
Bioaccumulative potential	No ecological damage caused by this product.

12.4. Mobility in soil

Nitrogen, refrigerated liquid (7727-37-9)	
Mobility in soil	No data available.
Ecology - soil	No ecological damage caused by this product.

12.5. Other adverse effects

Other adverse effects : Can cause frost damage to vegetation.

Effect on ozone layer : None

Effect on the global warming : No known effects from this product

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Waste disposal recommendations : Dispose of contents/container in accordance with local/regional/national/international regulations. Contact supplier for any special requirements.

SECTION 14: Transport information

In accordance with DOT

Transport document description : UN1977 Nitrogen, refrigerated liquid (cryogenic liquid), 2.2

UN-No.(DOT) : UN1977

Proper Shipping Name (DOT) : Nitrogen, refrigerated liquid
cryogenic liquid

Class (DOT) : 2.2 - Class 2.2 - Non-flammable compressed gas 49 CFR 173.115

Hazard labels (DOT) : 2.2 - Non-flammable gas

DOT Special Provisions (49 CFR 172.102)	:	345 - "Nitrogen, refrigerated liquid (cryogenic liquid), UN1977" transported in open cryogenic receptacles with a maximum capacity of 1 L are not subject to the requirements of this subchapter. The receptacles must be constructed with glass double walls having the space between the walls vacuum insulated and each receptacle must be transported in an outer packaging with sufficient cushioning and absorbent materials to protect the receptacle from damage 346 - "Nitrogen, refrigerated liquid (cryogenic liquid), UN1977" transported in accordance with the requirements for open cryogenic receptacles in §173.320 and this special provision are not subject to any other requirements of this subchapter. The receptacle must contain no hazardous materials other than the liquid nitrogen which must be fully absorbed in a porous material in the receptacle T75 - When portable tank instruction T75 is referenced in Column (7) of the 172.101 Table, the applicable refrigerated liquefied gases are authorized to be transported in portable tanks in accordance with the requirements of 178.277 of this subchapter TP5 - For a portable tank used for the transport of flammable refrigerated liquefied gases or refrigerated liquefied oxygen, the maximum rate at which the portable tank may be filled must not exceed the liquid flow capacity of the primary pressure relief system rated at a pressure not exceeding 120 percent of the portable tank's design pressure. For portable tanks used for the transport of refrigerated liquefied helium and refrigerated liquefied atmospheric gas (except oxygen), the maximum rate at which the tank is filled must not exceed the liquid flow capacity of the pressure relief device rated at 130 percent of the portable tank's design pressure. Except for a portable tank containing refrigerated liquefied helium, a portable tank shall have an outage of at least two percent below the inlet of the pressure relief device or pressure control valve, under conditions of incipient opening, with the portable tank in a level attitude. No outage is required for helium

Additional information

Emergency Response Guide (ERG) Number	:	121 (UN1066);120 (UN1977)
Other information	:	No supplementary information available.
Special transport precautions	:	Avoid transport on vehicles where the load space is not separated from the driver's compartment. Ensure vehicle driver is aware of the potential hazards of the load and knows what to do in the event of an accident or an emergency. Before transporting product containers: - Ensure there is adequate ventilation. - Ensure that containers are firmly secured. - Ensure cylinder valve is closed and not leaking. - Ensure valve outlet cap nut or plug (where provided) is correctly fitted. - Ensure valve protection device (where provided) is correctly fitted.

Transport by sea

UN-No. (IMDG)	:	1977
Proper Shipping Name (IMDG)	:	NITROGEN, REFRIGERATED LIQUID
Class (IMDG)	:	2.2 - Non-flammable, non-toxic gases
MFAG-No	:	120

Air transport

UN-No. (IATA)	:	1977
Proper Shipping Name (IATA)	:	NITROGEN, REFRIGERATED LIQUID
Class (IATA)	:	2
Civil Aeronautics Law	:	Gases under pressure/Gases nonflammable nontoxic under pressure

SECTION 15: Regulatory information

15.1. US Federal regulations

Nitrogen, refrigerated liquid (7727-37-9)	
Listed on the United States TSCA (Toxic Substances Control Act) inventory	
SARA Section 311/312 Hazard Classes	Immediate (acute) health hazard Sudden release of pressure hazard

All components of this product are listed on the Toxic Substances Control Act (TSCA) inventory.

This product or mixture does not contain a toxic chemical or chemicals in excess of the applicable de minimis concentration as specified in 40 CFR §372.38(a) subject to the reporting requirements of section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 and 40 CFR Part 372.

15.2. International regulations

CANADA

Nitrogen, refrigerated liquid (7727-37-9)
Listed on the Canadian DSL (Domestic Substances List)

EU-Regulations

Nitrogen, refrigerated liquid (7727-37-9)
Listed on the EEC inventory EINECS (European Inventory of Existing Commercial Chemical Substances)

15.2.2. National regulations

Nitrogen, refrigerated liquid (7727-37-9)
Listed on the AICS (Australian Inventory of Chemical Substances) Listed on IECSC (Inventory of Existing Chemical Substances Produced or Imported in China) Listed on the Korean ECL (Existing Chemicals List) Listed on NZIoC (New Zealand Inventory of Chemicals) Listed on PICCS (Philippines Inventory of Chemicals and Chemical Substances) Listed on INSQ (Mexican National Inventory of Chemical Substances)

15.3. US State regulations

Nitrogen, refrigerated liquid(7727-37-9)	
U.S. - California - Proposition 65 - Carcinogens List	No
U.S. - California - Proposition 65 - Developmental Toxicity	No
U.S. - California - Proposition 65 - Reproductive Toxicity - Female	No
U.S. - California - Proposition 65 - Reproductive Toxicity - Male	No
State or local regulations	U.S. - Massachusetts - Right To Know List U.S. - New Jersey - Right to Know Hazardous Substance List U.S. - Pennsylvania - RTK (Right to Know) List

California Proposition 65 - This product does not contain any substances known to the state of California to cause cancer, developmental and/or reproductive harm

SECTION 16: Other information

Other information : When you mix two or more chemicals, you can create additional, unexpected hazards. Obtain and evaluate the safety information for each component before you produce the mixture. Consult an industrial hygienist or other trained person when you evaluate the end product. Before using any plastics, confirm their compatibility with this product

Praxair asks users of this product to study this SDS and become aware of the product hazards and safety information. To promote safe use of this product, a user should (1) notify employees, agents, and contractors of the information in this SDS and of any other known product hazards and safety information, (2) furnish this information to each purchaser of the product, and (3) ask each purchaser to notify its employees and customers of the product hazards and safety information

The opinions expressed herein are those of qualified experts within Praxair, Inc. We believe that the information contained herein is current as of the date of this Safety Data Sheet. Since the use of this information and the conditions of use are not within the control of Praxair, Inc, it is the user's obligation to determine the conditions of safe use of the product

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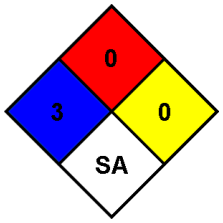
NFPA health hazard : 3 - Short exposure could cause serious temporary or residual injury even though prompt medical attention was given.

NFPA fire hazard : 0 - Materials that will not burn.

NFPA reactivity : 0 - Normally stable, even under fire exposure conditions, and are not reactive with water.

NFPA specific hazard : SA - This denotes gases which are simple asphyxiants.



HMIS III Rating

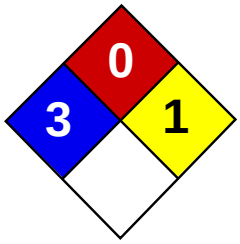
Health : 3 Serious Hazard - Major injury likely unless prompt action is taken and medical treatment is given

Flammability : 0 Minimal Hazard

Physical : 2 Moderate Hazard

SDS US (GHS HazCom 2012) - Praxair

This information is based on our current knowledge and is intended to describe the product for the purposes of health, safety and environmental requirements only. It should not therefore be construed as guaranteeing any specific property of the product.



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 flammble 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 Hydrodgen 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 AgClO + CCl4 Alcohols + hydrogen cyanide, Aluminum Aluminum-titanium alloys (with HCl vapor), 2-Amino ethanol, Ammonium hydroxide, Calcium carbide Ca3P2 Chlorine + dinitroanilines (evolves gas), Chlorosulfonic acid Cesium carbide Cesium acetylene carbide, 1,1-Difluoroethylene Ethylene diamine Ethylene imine, Fluorine, HClO4 Hexalithium disilicide H2SO4 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, U3P4 , 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 exothmeric reaction. Hydrogen chloride causes aldehydes and epoxides to violently polymerize. Hydrogen chloride or Hydrochloric Acid in contact with the folloiwng 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, platinium, 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 (fetoxicity). 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/conjuntivitis, 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 larryngeal burning, and irritation, pain and inflammation, coughing, sneezing, choking sensation, hoarseness, laryngeal spasms, upper respiratory tract edema, chest pains, as well has 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, vomitting (with "coffee ground" emesis), diarrhea, thirst, difficulty swallowing, salivation, chills, fever, uneasiness, shock, strictures and stenosis (esophogeal, 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 Indutrial 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 dangeureuses au canada. Centre de conformité internatinal Ltée. 1986.

Other Special Considerations: Not available.

Created: 10/09/2005 05:45 PM

Last Updated: 05/21/2013 12:00 PM

Material Safety Data Sheet for Cell Cultures
(Biosafety Level 1)

1. Product Identification

Name of cell line: CHO (CLS order no. 603479)
Designation: Chinese Hamster Ovary cell line, permanent cell line

2. Company Identification

CLS Cell Lines Service GmbH
Dr. Eckener-Str. 8
D-69214 Eppelheim
Germany

Emergency phone number: +49 (0)6221 700799

3. Composition / Ingredients

Unit: cryovial; frozen liquid

Hazardous Ingredient(s)	CAS no.	Percentage	EC no.
Dimethyl Sulfoxide	67-68-5	10	200-664-3

Non-Hazardous Ingredient(s)	Percentage
DMEM, supplemented for freezing	60-80
FBS (Fetal Bovine Serum)	10-20
Cells	1

4. Hazards Identification

Hamster source cell line
Categorized as non-infectious and non-toxic

5. First Aid Measures

Skin contact:
Wash off immediately with plenty of water and soap.
Eye contact:
Flush eyes immediately with water for 10-15 minutes.
Ingestion:
If the material was swallowed, rinse the mouth with water.

6. Accidental Release Measures

Use personal protective equipment
Do not flush into surface water.
Clean contaminated surface thoroughly. Autoclave before disposal into appropriated containers.

7. Handling and storage

Handling:
Open only under a sterile workbench. Wear protective equipment. Handle as if containing infectious material.
Storage:
Keep the cryovial at -150°C (freezer) or at -196°C (liquid nitrogen vapour phase).

8. Personal Protection

Hygienic measures
Avoid the contact with skin, eyes and clothing. Keep away from food and drinks. Wash hands immediately after handling the product.

Normally, no respiratory protective equipment is required.

Use protective gloves and safety goggles and wear a lab coat while handling the product.

9. Physical and Chemical Properties / Reactivity

Form:
Liquid

DMSO is stable. It is incompatible with a very wide range of materials, including acid chlorides, strong acids, strong oxidizing agents, strong reducing agents, phosphorus halides, moisture, copper wool + trichloroacetic acid, hygroscopic.

10. Toxicological Information

Not hazardous according to Directive 67/548/EC.

Toxicity data for DMSO:

ORL-RAT LD50 14500 mg kg^{-1}
IVN-MAN TDLO 686 mg kg^{-1}
IVN-MUS LD50 3100 mg kg^{-1}
IVN-DOG LD50 2500 mg kg
ORL-MAM LD50 21400 mg kg^{-1}
IPR-RAT LD50 8200 mg kg^{-1}
ORL-BWD LD50 100 mg kg^{-1}

11. Transportation Information

Non-hazardous for air, sea and road freight.

12. General Information

Recommended use:
For in vitro research use only.

Disclaimer:
The information provided in the present Material Safety Data Sheet is believed to be correct at the date of publication. No guarantee is given for its accuracy or completeness, but is intended as guidance only. Biological material may be hazardous and should be used with caution.
CLS Cell Lines Service GmbH shall not be held liable for any damage resulting from handling or from contact with the product.

CLS Cell Lines Service GmbH, Dr. Eckener-Straße 8, 69214 Eppelheim, Germany
TEL: +49(0)6221 700799 FAX +49(0)6221 700717 info@clsgmbh.de www.clsgmbh.de

SAFETY DATA SHEET

Creation Date 30-Apr-2010 **Revision Date** 17-Jan-2018 **Revision Number** 4

1. Identification

Product Name **Sodium hypochlorite**

Cat No. : **SS290-1; SS290-4; SS290-4LC**

Synonyms No information available

Recommended Use Laboratory chemicals.
Uses advised against Not for food, drug, pesticide or biocidal product use

Details of the supplier of the safety data sheet

Company
Fisher Scientific
One Reagent Lane
Fair Lawn, NJ 07410
Tel: (201) 796-7100

Emergency Telephone Number
CHEMTREC®, Inside the USA: 800-424-9300
CHEMTREC®, Outside the USA: 001-703-527-3887

2. Hazard(s) identification

Classification
This chemical is considered hazardous by the 2012 OSHA Hazard Communication Standard (29 CFR 1910.1200)

Corrosive to metals	Category 1
Skin Corrosion/irritation	Category 2
Serious Eye Damage/Eye Irritation	Category 1
Specific target organ toxicity (single exposure)	Category 3
Target Organs - Respiratory system.	

Label Elements

Signal Word
Danger

Hazard Statements
May be corrosive to metals
Causes severe skin burns and eye damage
May cause respiratory irritation

Precautionary Statements
Prevention
Wash face, hands and any exposed skin thoroughly after handling
Wear protective gloves/protective clothing/eye protection/face protection
Avoid breathing dust/fume/gas/mist/vapors/spray
Use only outdoors or in a well-ventilated area
Keep only in original container
Inhalation
IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing
Call a POISON CENTER or doctor/physician if you feel unwell
Skin
IF ON SKIN: Wash with plenty of soap and water
If skin irritation occurs: Get medical advice/attention
Take off contaminated clothing and wash before reuse
Eyes
IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
Immediately call a POISON CENTER or doctor/physician
Spills
Absorb spillage to prevent material damage
Storage
Store in a well-ventilated place. Keep container tightly closed
Store locked up
Store in corrosive resistant polypropylene container with a resistant inliner
Store in a dry place
Disposal
Dispose of contents/container to an approved waste disposal plant
Hazards not otherwise classified (HNOC)
Toxic to aquatic life with long lasting effects
Contact with acids liberates toxic gas

3. Composition/Information on Ingredients

Component	CAS-No	Weight %
Water	7732-18-5	94-96
Sodium hypochlorite	7681-52-9	4-6

4. First-aid measures

General Advice Immediate medical attention is required. Show this safety data sheet to the doctor in attendance.

Eye Contact Rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. Immediate medical attention is required. Keep eye wide open while rinsing.

Skin Contact Wash off immediately with plenty of water for at least 15 minutes. Remove and wash contaminated clothing before re-use. Call a physician immediately.

Inhalation If breathing is difficult, give oxygen. Do not use mouth-to-mouth method if victim ingested or inhaled the substance; give artificial respiration with the aid of a pocket mask equipped with a one-way valve or other proper respiratory medical device. Remove from exposure, lie down. Call a physician immediately.

Ingestion Do not induce vomiting. Never give anything by mouth to an unconscious person. Clean mouth with water. Call a physician immediately.

Most important symptoms and Causes eye burns. Causes burns by all exposure routes. . Product is a corrosive material.

effects Use of gastric lavage or emesis is contraindicated. Possible perforation of stomach or esophagus should be investigated: Ingestion causes severe swelling, severe damage to the delicate tissue and danger of perforation

Notes to Physician Treat symptomatically

5. Fire-fighting measures

Suitable Extinguishing Media CO_2, dry chemical, dry sand, alcohol-resistant foam.

Unsuitable Extinguishing Media No information available

Flash Point Not applicable
Method - No information available

Autoignition Temperature No information available
Explosion Limits
Upper No data available
Lower No data available
Sensitivity to Mechanical Impact No information available
Sensitivity to Static Discharge No information available

Specific Hazards Arising from the Chemical
Thermal decomposition can lead to release of irritating gases and vapors. The product causes burns of eyes, skin and mucous membranes. Do not allow run-off from fire fighting to enter drains or water courses.

Hazardous Combustion Products
Hydrogen chloride gas Sodium oxides Thermal decomposition can lead to release of irritating gases and vapors
Protective Equipment and Precautions for Firefighters
As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear. Thermal decomposition can lead to release of irritating gases and vapors.

NFPA

Health	Flammability	Instability	Physical hazards
3	0	1	N/A

6. Accidental release measures

Personal Precautions Ensure adequate ventilation. Use personal protective equipment. Keep people away from and upwind of spill/leak. Evacuate personnel to safe areas.

Environmental Precautions Do not flush into surface water or sanitary sewer system. Do not allow material to contaminate ground water system. Prevent product from entering drains. Local authorities should be advised if significant spillages cannot be contained. See Section 12 for additional ecological information. Avoid release to the environment. Collect spillage.

Methods for Containment and Clean Up Soak up with inert absorbent material. Keep in suitable, closed containers for disposal.

7. Handling and storage

Handling Use only under a chemical fume hood. Wear personal protective equipment. Do not get in eyes, on skin, or on clothing. Do not ingest. Do not breathe vapors or spray mist.

Storage Keep containers tightly closed in a dry, cool and well-ventilated place. Corrosives area.

8. Exposure controls / personal protection

Exposure Guidelines This product does not contain any hazardous materials with occupational exposure limitsestablished by the region specific regulatory bodies.

Engineering Measures Use only under a chemical fume hood. Ensure that eyewash stations and safety showers are close to the workstation location.

Personal Protective Equipment

Eye/face Protection 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. Tightly fitting safety goggles. Face-shield.

Skin and body protection Long sleeved clothing.

Respiratory Protection 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.

Hygiene Measures Handle in accordance with good industrial hygiene and safety practice.

9. Physical and chemical properties

Physical State	Liquid
Appearance	Light yellow
Odor	Chlorine
Odor Threshold	No information available
pH	No information available
Melting Point/Range	0 °C / 32 °F
Boiling Point/Range	No information available
Flash Point	Not applicable
Evaporation Rate	> 1 (Ether = 1.0)
Flammability (solid,gas)	Not applicable
Flammability or explosive limits	
Upper	No data available
Lower	No data available
Vapor Pressure	14 mmHg
Vapor Density	No information available
Specific Gravity	1.1
Solubility	Soluble in water
Partition coefficient; n-octanol/water	No data available
Autoignition Temperature	No information available
Decomposition Temperature	No information available
Viscosity	No information available
Molecular Formula	NaOCl
Molecular Weight	75.4492

10. Stability and reactivity

Reactive Hazard Yes

Stability Stable under normal conditions.

Conditions to Avoid Incompatible products. Excess heat.

Incompatible Materials Strong oxidizing agents, Strong acids, Strong bases, Strong reducing agents

Hazardous Decomposition Products Hydrogen chloride gas, Sodium oxides, Thermal decomposition can lead to release of irritating gases and vapors

Hazardous Polymerization Hazardous polymerization does not occur.

Hazardous Reactions None under normal processing.

11. Toxicological information

Acute Toxicity

Product Information

Oral LD50 Based on ATE data, the classification criteria are not met. ATE > 2000 mg/kg.

Dermal LD50 Based on ATE data, the classification criteria are not met. ATE > 2000 mg/kg.

Vapor LC50 Based on ATE data, the classification criteria are not met. ATE > 20 mg/l.

Component Information

Component	LD50 Oral	LD50 Dermal	LC50 Inhalation
Water	-	Not listed	Not listed
Sodium hypochlorite	LD50 = 8200 mg/kg (Rat)	LD50 > 10000 mg/kg (Rabbit)	> 10500 mg/l (Rat) 1h

Toxicologically Synergistic Products No information available

Delayed and immediate effects as well as chronic effects from short and long-term exposure

Irritation Causes burns by all exposure routes

Sensitization No information available

Carcinogenicity The table below indicates whether each agency has listed any ingredient as a carcinogen.

Component	CAS-No	IARC	NTP	ACGIH	OSHA	Mexico
Water	7732-18-5	Not listed	Not listed	Not listed	Not listed	Not listed
Sodium hypochlorite	7681-52-9	Not listed	Not listed	Not listed	Not listed	Not listed

Mutagenic Effects No information available

Reproductive Effects No information available.

Developmental Effects No information available.

Teratogenicity No information available.

STOT - single exposure Respiratory system

STOT - repeated exposure None known

Aspiration hazard No information available

Symptoms / effects,both acute and delayed Product is a corrosive material. Use of gastric lavage or emesis is contraindicated. Possible perforation of stomach or esophagus should be investigated: Ingestion causes severe swelling, severe damage to the delicate tissue and danger of perforation

Endocrine Disruptor Information No information available

Other Adverse Effects The toxicological properties have not been fully investigated.

12. Ecological information

Ecotoxicity

The product contains following substances which are hazardous for the environment. Very toxic to aquatic organisms.

Component	Freshwater Algae	Freshwater Fish	Microtox	Water Flea
Sodium hypochlorite	EC50: = 0.095 mg/L, 24h (Skeletonema costatum)	Pimephales promelas: LC50=0.82-0.98 mg/L 96h	-	2.1 mg/L EC50 = 96 h 0.033-0.044 mg/L EC50 48 h

Persistence and Degradability No information available

Bioaccumulation/ Accumulation No information available.

Mobility .

13. Disposal considerations

Waste Disposal Methods Chemical waste generators must determine whether a discarded chemical is classified as a hazardous waste. Chemical waste generators must also consult local, regional, and national hazardous waste regulations to ensure complete and accurate classification.

14. Transport information

DOT

UN-No	UN1791
Proper Shipping Name	HYPOCHLORITE SOLUTIONS
Hazard Class	8
Packing Group	III

TDG

UN-No	UN1791
Proper Shipping Name	HYPOCHLORITE SOLUTION
Hazard Class	8
Packing Group	III

IATA

UN-No	UN1791
Proper Shipping Name	HYPOCHLORITE SOLUTION
Hazard Class	8
Packing Group	III

IMDG/IMO

UN-No	UN1791
Proper Shipping Name	HYPOCHLORITE SOLUTION
Hazard Class	8
Packing Group	III

15. Regulatory information

All of the components in the product are on the following Inventory lists: X = listed

International Inventories

Component	TSCA	DSL	NDSL	EINECS	ELINCS	NLP	PICCS	ENCS	AICS	IECSC	KECL
Water	X	X	-	231-791-2	-		X	-	X	X	X
Sodium hypochlorite	X	X	-	231-668-3	-		X	X	X	X	X

Legend:
X - Listed
E - Indicates a substance that is the subject of a Section 5(e) Consent order under TSCA.
F - Indicates a substance that is the subject of a Section 5(f) Rule under TSCA.
N - Indicates a polymeric substance containing no free-radical initiator in its inventory name but is considered to cover the designated polymer made with any free-radical initiator regardless of the amount used.
P - Indicates a commenced PMN substance
R - Indicates a substance that is the subject of a Section 6 risk management rule under TSCA.
S - Indicates a substance that is identified in a proposed or final Significant New Use Rule
T - Indicates a substance that is the subject of a Section 4 test rule under TSCA.
XU - Indicates a substance exempt from reporting under the Inventory Update Rule, i.e. Partial Updating of the TSCA Inventory Data Base Production and Site Reports (40 CFR 710(B).
Y1 - Indicates an exempt polymer that has a number-average molecular weight of 1,000 or greater.
Y2 - Indicates an exempt polymer that is a polyester and is made only from reactants included in a specified list of low concern reactants that comprises one of the eligibility criteria for the exemption rule.

U.S. Federal Regulations

TSCA 12(b) Not applicable

SARA 313 Not applicable

SARA 311/312 Hazard Categories See section 2 for more information

CWA (Clean Water Act)

Component	CWA - Hazardous Substances	CWA - Reportable Quantities	CWA - Toxic Pollutants	CWA - Priority Pollutants
Sodium hypochlorite	X	100 lb	-	-

Clean Air Act Not applicable

OSHA Occupational Safety and Health Administration
Not applicable

CERCLA Not applicable

Component	Hazardous Substances RQs	CERCLA EHS RQs
Sodium hypochlorite	100 lb	-

California Proposition 65 This product does not contain any Proposition 65 chemicals

U.S. State Right-to-Know Regulations

Component	Massachusetts	New Jersey	Pennsylvania	Illinois	Rhode Island
Water	-	-	X	-	-
Sodium hypochlorite	X	X	X	-	-

U.S. Department of Transportation

Reportable Quantity (RQ): N
DOT Marine Pollutant N
DOT Severe Marine Pollutant N

U.S. Department of Homeland Security
This product does not contain any DHS chemicals.

Other International Regulations

Mexico - Grade No information available

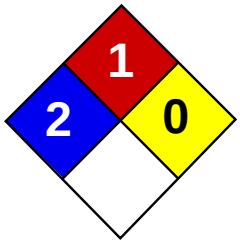
16. Other information

Prepared By Regulatory Affairs
Thermo Fisher Scientific
Email: EMSDS.RA@thermofisher.com

Creation Date 30-Apr-2010
Revision Date 17-Jan-2018
Print Date 17-Jan-2018
Revision Summary This document has been updated to comply with the US OSHA HazCom 2012 Standard replacing the current legislation under 29 CFR 1910.1200 to align with the Globally Harmonized System of Classification and Labeling of Chemicals (GHS).

Disclaimer
The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text

End of SDS



Material Safety Data Sheet
Ammonium sulfate MSDS

Section 1: Chemical Product and Company Identification

Product Name: Ammonium sulfate

Catalog Codes: SLA2851, SLA2011, SLA1168, SLA2674

CAS#: 7783-20-2

RTECS: BS4500000

TSCA: TSCA 8(b) inventory: Ammonium sulfate

CI#: Not available.

Synonym: Sulfluric Acid, Diammonium Salt

Chemical Name: Ammonium Sulfate

Chemical Formula: (NH4)2SO4

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
Ammonium sulfate	7783-20-2	100

Toxicological Data on Ingredients: Ammonium sulfate: ORAL (LD50): Acute: 2840 mg/kg [Rat]. 640 mg/kg [Mouse].

Section 3: Hazards Identification

Potential Acute Health Effects: 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.

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:
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.

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: Higher than 93.3°C (200°F).

Flammable Limits: Not available.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances:
Flammable in presence of oxidizing materials. 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. Explosive in presence of oxidizing materials.

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:
A mixture of ammonium sulfate and potassium chlorate decomposes with incandescence when heated. When a little ammonium sulfate is added to fused potassium nitrite, a vigorous reaction occurs attended by flame. Non combustible. This substance itself does not burn, but may decompose upon heating to produce corrosive and/or toxic fumes.

Special Remarks on Explosion Hazards:
If accidently mixed with oxidizers like potassium chlorate, potassium nitrate or potassium nitrite, there is an explosion hazard during fire. A mixture of ammonium sulfate and ammonium nitrate can easily be exploded by potassium or sodium-potassium alloy.

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 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. Avoid contact with skin and eyes. 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:
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. (Crystals solid.)

Odor: Odorless.

Taste: Not available.

Molecular Weight: 132.14 g/mole

Color: brownish gray to white

pH (1% soln/water): Not available.

Boiling Point: Not available.

Melting Point: 280°C (536°F)

Critical Temperature: Not available.

Specific Gravity: 1.77 (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. Insoluble in acetone.

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:
Highly reactive with oxidizing agents. Reactive with alkalis.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity:
Incompatible with the following: Potassium + ammonium nitrate, potassium chlorate, potassium nitrate, potassium nitrite, sodium hypochlorite, sodium/potassium alloy + ammonium nitrate. Substance should not contact either zinc or copper bearing materials. Reacts with alkali to release ammonia.

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): 640 mg/kg [Mouse].

Chronic Effects on Humans: Not available.

Other Toxic Effects on Humans: Hazardous in case of skin contact (irritant), of ingestion, of inhalation.

Special Remarks on Toxicity to Animals:
Lowest Published Lethal Dose/Conc: LDL [Domestic animal - Goat, Sheep) - Route: Oral; Dose: 3500 mg/kg

Special Remarks on Chronic Effects on Humans:
It may be a possible mutagen. It has been tested for mutagenicity, but so far tests have been inconclusive or test information has not been made available.

Special Remarks on other Toxic Effects on Humans:
Acute Potential Health Effects: Skin: Causes skin irritation. Eyes: Causes eye irritation. Inhalation: May cause respiratory tract irritation. Ingestion: When ingested, its osmolarity can draw water from the body into the bowel, acting as a laxative. However, if enough is absorbed systemically it may produce Ammonia poisoning. Symptoms may include gastrointestinal (digestive) tract irritation with nausea, vomiting, hypermotility, diarrhea. May also affect eyes (Mydriasis), behavior/central nervous system (somnolence, tremor, convulsions, muscle contraction or spasticity), and respiratory system (respiratory stimulation, dyspnea). Also, with ingestion of large doses of Ammonium Sulfate arises the possibility of sufficient absorption to produce diuresis, an excessive discharge of urine, and kidney damage (renal tubular disorder, abnormal renal function). Chronic Potential Health Effects: One Russian occupational standard study discussed chronic exposure effects which may include cardiac contraction, neurotoxicity, and hypertension. This has not been confirmed in other ammonium sulfate exposed workers.

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:
Rhode Island RTK hazardous substances: Ammonium sulfate Pennsylvania RTK: Ammonium sulfate Florida: Ammonium sulfate Massachusetts RTK: Ammonium sulfate New Jersey: Ammonium sulfate TSCA 8(b) inventory: Ammonium sulfate

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):
R16- Explosive when mixed with oxidizing substances. R36/38- Irritating to eyes and skin. S24/25- Avoid contact with skin and 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

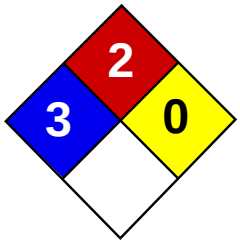
References: Not available.

Other Special Considerations: Not available.

Created: 10/10/2005 08:14 PM

Last Updated: 05/21/2013 12:00 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



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: C2-H4-O2

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 produces 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 phorphorus 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, abdomial spasms, vomiting, hematemesis, diarrhea. May Also affect the liver (impaired liver function), behavior (convulsions, giddines, 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 Subtances (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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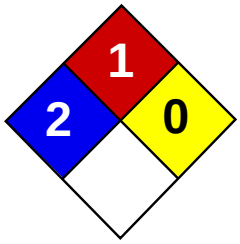
The information above is believed to be accurate and represents the best information currently available to us. However, we make no warranty of merchantability or any other warranty, express or implied, with respect to such information, and we assume



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 wth 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 Indutrial Materials. Toronto, Van Nostrand Reinold, 6e ed. 1984. -The Sigma-Aldrich Library of Chemical Safety Data, Edition II. Registery of Toxic Effects of Chemical Substances. Hazardous Substance Data Bank.

Other Special Considerations: Not available.

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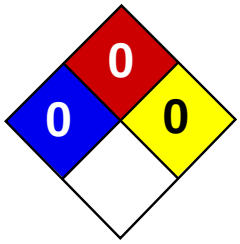

Health	0
Fire	0
Reactivity	0
Personal Protection	A

Material Safety Data Sheet
Water MSDS

Section 1: Chemical Product and Company Identification

Product Name: Water

Catalog Codes: SLW1063

CAS#: 7732-18-5

RTECS: ZC0110000

TSCA: TSCA 8(b) inventory: Water

CI#: Not available.

Synonym: Dihydrogen oxide

Chemical Name: Water

Chemical Formula: 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
Water	7732-18-5	100

Toxicological Data on Ingredients: Not applicable.

Section 3: Hazards Identification

Potential Acute Health Effects:
Non-corrosive for skin. Non-irritant for skin. Non-sensitizer for skin. Non-permeator by skin. Non-irritating to the eyes. Non-hazardous in case of ingestion. Non-hazardous in case of inhalation. Non-irritant for lungs. Non-sensitizer for lungs. Non-corrosive to the eyes. Non-corrosive for lungs.

Potential Chronic Health Effects:
Non-corrosive for skin. Non-irritant for skin. Non-sensitizer for skin. Non-permeator by skin. Non-irritating to the eyes. Non-hazardous in case of ingestion. Non-hazardous in case of inhalation. Non-irritant for lungs. Non-sensitizer for lungs. CARCINOGENIC EFFECTS: Not available. MUTAGENIC EFFECTS: Not available. TERATOGENIC EFFECTS: Not available. DEVELOPMENTAL TOXICITY: Not available.

Section 4: First Aid Measures

Eye Contact: Not applicable.

Skin Contact: Not applicable.

Serious Skin Contact: Not available.

Inhalation: Not applicable.

Serious Inhalation: Not available.

Ingestion: Not Applicable

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: Not Applicable

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: Mop up, or absorb with an inert dry material and place in an appropriate waste disposal container.

Large Spill: Absorb with an inert material and put the spilled material in an appropriate waste disposal.

Section 7: Handling and Storage

Precautions: No specific safety phrase has been found applicable for this product.

Storage: Not applicable.

Section 8: Exposure Controls/Personal Protection

Engineering Controls: Not Applicable

Personal Protection: Safety glasses. Lab coat.

Personal Protection in Case of a Large Spill: Not Applicable

Exposure Limits: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Liquid.

Odor: Odorless.

Taste: Not available.

Molecular Weight: 18.02 g/mole

Color: Colorless.

pH (1% soln/water): 7 [Neutral.]

Boiling Point: 100°C (212°F)

Melting Point: Not available.

Critical Temperature: Not available.

Specific Gravity: 1 (Water = 1)

Vapor Pressure: 2.3 kPa (@ 20°C)

Vapor Density: 0.62 (Air = 1)

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: Not applicable

Solubility: Not Applicable

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: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Absorbed through skin. Eye contact.

Toxicity to Animals:
LD50: [Rat] - Route: oral; Dose: > 90 ml/kg LC50: Not available.

Chronic Effects on Humans: Not available.

Other Toxic Effects on Humans:
Non-corrosive for skin. Non-irritant for skin. Non-sensitizer for skin. Non-permeator by skin. Non-hazardous in case of ingestion. Non-hazardous in case of inhalation. Non-irritant for lungs. Non-sensitizer for lungs. Non-corrosive to the eyes. Non-corrosive for lungs.

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 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: Water

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: 0

Fire Hazard: 0

Reactivity: 0

Personal Protection: a

National Fire Protection Association (U.S.A.):

Health: 0

Flammability: 0

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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Conforms to 93/112/EC and ISO 11014-1

SAFETY DATA SHEET

Order Number

Customer Number

1. Identification of the substance/preparation and of the company/undertaking

Product name : **Tris Base, Molecular Biology Grade**

Chemical formula : $C_4H_{11}NO_3$

Synonym : tris(Hydroxymethyl)aminomethane; 1,3-Propanediol, 2-amino-2-(hydroxymethyl)-

Catalog # : 648310

Supplier : Manufactured by EMD Biosciences, Inc.
10394 Pacific Center Court
San Diego, CA 92121
(858)450-5558/(800)854-3417
FAX: (858)453-3552

Emergency telephone number : **Call Chemtrec®**
(800)424-9300 (within U.S.A.)
(703)527-3887 (outside U.S.A.)

2. Composition / information on ingredients

Substance/Preparation : Substance

Chemical name*	CAS No.	EC Number	Symbol	R-Phrases
1) tris(Hydroxymethyl)aminomethane; 1,3-Propanediol, 2-amino-2-(hydroxymethyl)-	77-86-1	201-064-4	Xi	R36/38

3. Hazards identification

Physical/chemical hazards : Not applicable.

Human health hazards : CAUTION!
MAY CAUSE EYE AND SKIN IRRITATION.

4. First-aid measures

First-Aid measures

Inhalation : If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get 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.

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.

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.

Effects and symptoms

Skin Contact : Hazardous in case of skin contact (irritant). Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering.

Eye Contact : Hazardous in case of eye contact (irritant).

Aggravating conditions : Repeated or prolonged exposure is not known to aggravate medical condition.

5. Fire-fighting measures

Flammability of the Product : May be combustible at high temperature.

Extinguishing Media

Suitable : SMALL FIRE: Use DRY chemical powder.
LARGE FIRE: Use water spray, fog or foam. Do not use water jet.

Hazardous thermal (de)composition products : These products are carbon oxides (CO, CO2), nitrogen oxides (NO, NO2...).

Special fire-fighting procedures : Fire fighters should wear positive pressure self-contained breathing apparatus (SCBA) and full turnout gear.

Protection of fire-fighters : Be sure to use an approved/certified respirator or equivalent.

6. Accidental release measures

Personal precautions : 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.

Small Spill and Leak : 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 and Leak : 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 systen

7. Handling and storage

Handling : 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. 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, alkalis.

Storage : Keep container tightly closed. Keep container in a cool, well-ventilated area. Do not store above 20°C (68°F).

Packaging materials

Recommended use : Use original container.

8. Exposure controls/personal protection

Engineering measures : 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.

Hygiene measures : Wash hands after handling compounds and before eating, smoking, using lavatory, and at the end of day.

Ingredient Name	Occupational Exposure Limits
1) Tris Base, Molecular Biology Grade	Not available.

Personal protective equipment

Respiratory system : Dust respirator. Be sure to use an approved/certified respirator or equivalent.

Skin and body : Lab coat.

Hands : Gloves.

Eyes : Splash goggles.

Protective Clothing (Pictograms) :

9. Physical and chemical properties

Physical state : Solid. (Solid crystalline powder.)

Color : White.

Molecular Weight : 121.1 g/mole

Melting Point : 171.2 to 172.3°C (340.2 to 342.1°F)

Solubility : Easily soluble in cold water.

Flash point : Not available.

Explosive properties : 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.

10. Stability and reactivity

Stability : The product is stable.

Conditions to avoid : Not available.

Materials to avoid : Reactive with oxidizing agents, alkalis.

Hazardous Decomposition Products : These products are carbon oxides (CO, CO2), nitrogen oxides (NO, NO2...).

11. Toxicological information

RTECS # : **TY2900000**

Local effects

Skin irritation : Hazardous in case of skin contact (irritant).

Acute toxicity : LD50: Not available.
LC50: Not available.

Chronic toxicity : Repeated or prolonged exposure is not known to aggravate medical condition.

Other Toxic Effects on Humans : Not available.
Hazardous in case of skin contact (irritant).

Not available.

Not available.

Carcinogenic effects : Not available.

Mutagenic effects : Not available.

Reproduction toxicity : Not available.

Teratogenic effects : Not available.

12. Ecological information

Ecotoxicity : Not available.

Toxicity of the Products of Biodegradation : The product itself and its products of degradation are not toxic.

13. Disposal considerations

Methods of disposal; Waste of residues; Contaminated packaging : Waste must be disposed of in accordance with federal, state and local environmental control regulations.

14. Transport information

International transport regulations

Land - Road/Railway

ADR/RID Class : Not controlled under ADR (Europe).

Sea

IMDG Class : Not controlled under IMDG.

Air

IATA-DGR Class : Not controlled under IATA.

Special Provisions for Transport Not applicable.

15. Regulatory information

EU Regulations

Hazard symbol(s) :

Classification : Irritant

Risk Phrases : R36/38- Irritating to eyes and skin.

Safety Phrases : S26- In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

U.S. Federal Regulations : TSCA 8(b) inventory: Tris Base, Molecular Biology Grade
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.
SARA 313 toxic chemical notification and release reporting: 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.

HCS Classification : CLASS: Irritating substance.

State Regulations :

WHMIS (Canada) : Not controlled under WHMIS (Canada).

CEPA DSL: Tris Base, Molecular Biology Grade

16. Other information

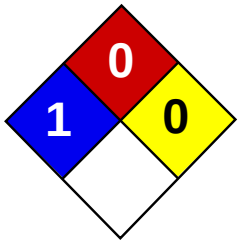
Hazardous Material Information System (U.S.A.)

Health	2
Fire Hazard	1
Reactivity	0
Personal Protection	E

National Fire Protection Association (U.S.A.)

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.



Material Safety Data Sheet
Sodium phosphate, dibasic MSDS

Section 1: Chemical Product and Company Identification

Product Name: Sodium phosphate, dibasic

Catalog Codes: SLS2365, SLS2986, SLS4408

CAS#: 7558-79-4

RTECS: WC4500000

TSCA: TSCA 8(b) inventory: Sodium phosphate, dibasic

CI#: Not available.

Synonym: Dibasic Sodium Phosphate; Disodium hydrogen phosphate; Disodium monohydrogen phosphate; Disodium orthophosphate; Disodium phosphoric acid; Phosphoric acid, disodium salt; Soda phosphate; Sodium hydrogen phosphate

Chemical Name: Sodium Monohydrogen Phosphate(2:1:1)

Chemical Formula: Na2HPO4

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, dibasic	7558-79-4	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: 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.

Section 7: Handling and Storage

Precautions:
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 acids, alkalis.

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: 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. (Solid powder.)

Odor: Odorless.

Taste: Saline.

Molecular Weight: 141.96 g/mole

Color: White.

pH (1% soln/water): 9.1 [Basic.]

Boiling Point: Not available.

Melting Point:
Decomposition temperature: 240°C (464°F) Converted to Sodium Pyrophosphate @ about 240 deg. C

Critical Temperature: Not available.

Specific Gravity: Not available.

Vapor Pressure: Not applicable.

Vapor Density: 4.9 (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. Insoluble in methanol, n-octanol.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability:

Exposure to moisture and to incompatible materials. When heated to decompostition, it emits toxic fumes of phosphoxides and sodium oxide.

Incompatibility with various substances: Reactive with acids, alkalis.

Corrosivity: Not available.

Special Remarks on Reactivity:
Hygroscopic; keep container tightly closed. Incompatible with magnesium, alkaloids, antipyrine, chloral hydrate, lead acetate, pyrogallol, resorcinol, strong mineral acids, strong organic acids.

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): 17000 mg/kg [Rat].

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: Causes mild skin irritation. May cause dermatitis. Eyes: Causes mild eye irritation. Ingestion: May cause irritation of the digestive tract and may cause purging. It is slowly aborbed. Expected to be a low ingestion hazard for usual industrial handling. Ingestion of large doses may affect behavior/central nervous system (tetany). However, if a significant amount of phosphate is absorbed, hypophosphatemia will occur. Severe hypophosphatemia may result in hypocalcemia and tetany. Cardiovasular, respiratory, neurologic, and musculoskeletal effects may occur secondary to hypernatremia, hypophosphatemia, and hypocalcemia Inhalation: May cause respiratory tract and mucous membrane irritation. Low hazard for usual industrial handling. Chronic Potential Health Effects: Skin: High and repeated exposure may cause dermatitis.

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 available. UNNA: 9147 PG: III

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations:
New York release reporting list: Sodium phosphate, dibasic Pennsylvania RTK: Sodium phosphate, dibasic Massachusetts RTK: Sodium phosphate, dibasic New Jersey: Sodium phosphate, dibasic California Director's List of Hazardous Sustances: Sodium phosphate, dibasic TSCA 8(b) inventory: Sodium phosphate, dibasic CERCLA: Hazardous substances.: Sodium phosphate, dibasic: 5000 lbs. (2268 kg)

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. 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. Safety glasses.

Section 16: Other Information

References: -Hawley, G.G.. The Condensed Chemical Dictionary, 11e ed., New York N.Y., Van Nostrand Reinold, 1987.

Other Special Considerations: Not available.

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Last Updated: 05/21/2013 12:00 PM

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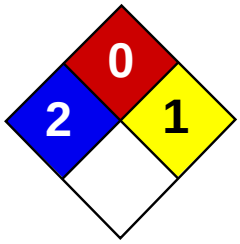

Material Safety Data Sheet
Sodium carbonate monohydrate MSDS

Section 1: Chemical Product and Company Identification

Product Name: Sodium carbonate monohydrate

Catalog Codes: SLS1099, SLS2521, SLS3943

CAS#: 5968-11-6

RTECS: Not available.

TSCA: TSCA 8(b) inventory: No products were found.

CI#: Not available.

Synonym: Disodium Carbonate monohydrate

Chemical Name: Carbonic Acid, disodium salt, monohydrate

Chemical Formula: Na2CO3.H20

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 carbonate monohydrate	5968-11-6	100

Toxicological Data on Ingredients: Sodium carbonate monohydrate: DUST (LC50): Acute: 468 mg/m 4 hours [Guinea pig].

Section 3: Hazards Identification

Potential Acute Health Effects:
Hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation (lung irritant). 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. Severe over-exposure can produce lung damage, choking, unconsciousness or death.

Potential Chronic Health Effects:
Slightly hazardous in case of skin contact (irritant). CARCINOGENIC EFFECTS: Not available. MUTAGENIC EFFECTS: Not available. TERATOGENIC EFFECTS: Not available. DEVELOPMENTAL TOXICITY: Not available. The substance may be toxic to 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.

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:
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.

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: 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: 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. 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. Finish cleaning by spreading water on the contaminated surface and allow to evacuate through the sanitary system.

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.

Storage: Hygroscopic. 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:
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: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid. (Granular solid.)

Odor: Odorless.

Taste: Not available.

Molecular Weight: 124 g/mole

Color: White.

pH (1% soln/water): 11.6 [Basic.]

Boiling Point: Not available.

Melting Point: Not available.

Critical Temperature: Not available.

Specific Gravity: Density: 2.25 (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 hot water. Partially soluble in cold water. Soluble in 3 parts of cold water. Soluble in 1.8 parts of boiling water. Insoluble in alcohol. Soluble in 7 parts of glycero

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Incompatible materials, moisture

Incompatibility with various substances:
Reactive with acids. Slightly reactive to reactive with moisture.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity:
Hygroscopic; keep container tightly closed. Incompatible with aluminum and fluorine. Dries out somewhat in warm, dry air or above 50 C and becomes anhydrous at 100 C.

Special Remarks on Corrosivity: Not available.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Dermal contact. Inhalation. Ingestion.

Toxicity to Animals:
WARNING: THE LC50 VALUES HEREUNDER ARE ESTIMATED ON THE BASIS OF A 4-HOUR EXPOSURE. Acute toxicity of the dust (LC50): 468 mg/m 4 hours [Guinea pig]. 3

Chronic Effects on Humans: May cause damage to the following organs: upper respiratory tract, skin, eyes.

Other Toxic Effects on Humans: Hazardous in case of skin contact (irritant), of ingestion, of inhalation (lung irritant).

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: May cause adverse reproductive effects based on animal test data

Special Remarks on other Toxic Effects on Humans:
Acute Potential Health Effects: Skin: Causes skin irritation with possible burns depending on the concentration, site (abraded or intact skin), and duration of exposure. Eyes: Causes eye irritation and possible burns. May cause chemical conjunctivitis. Concentrated solutions may cause permanent corneal injury (permanent corneal opacity). Ingestion: Sodium carbonate ingestion may cause irritation of the digestive tract resulting in nausea, vomiting, diarrhea, thrist, abdominal pain depending on concentration and amount ingested. May also affect the cardiovascular system . Inhalation: Dust may cause respiratory tract and mucous membrane irritation with coughing and shortness of breath (dyspnea), pulmonary edema. Chronic Potential Health Effects: Chronic inhalation may result in decreased pulmonary function, nasal congestion, nosebleeds, perforation of the nasal septum. Other effects of chronic exposure are skin (dermatitis and ulceration), and gastrointestinal complaints. However, the effects of chronic exposure seem to be reversible if exposure is decreased.

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: 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: OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

Other Classifications:

WHMIS (Canada):
CLASS D-1A: Material causing immediate and serious toxic effects (VERY TOXIC). CLASS E: Corrosive solid.

DSCL (EEC):
R36/37/38- Irritating to eyes, respiratory system and skin. S22- Do not breathe dust. S26- In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

HMIS (U.S.A.):

Health Hazard: 2

Fire Hazard: 0

Reactivity: 1

Personal Protection: j

National Fire Protection Association (U.S.A.):

Health: 2

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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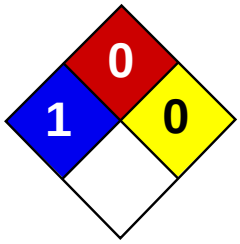

Health	1
Fire	0
Reactivity	0
Personal Protection	E

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, adn 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 affects 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, hypochloremia, 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, adn 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: 05/21/2013 12:00 PM

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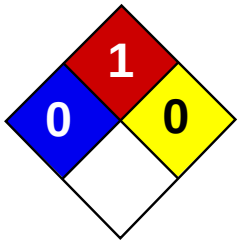

Material Safety Data Sheet
Propylene glycol MSDS

Section 1: Chemical Product and Company Identification

Product Name: Propylene glycol

Catalog Codes: SLP1162, SLP2974

CAS#: 57-55-6

RTECS: TY2000000

TSCA: TSCA 8(b) inventory: Propylene glycol

CI#: Not applicable.

Synonym: 1,2,-propanediol, 1,2-dihydroxypropane

Chemical Name: Propylene Glycol

Chemical Formula: CH3CHOHCH2OH

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
Propylene glycol	57-55-6	100

Toxicological Data on Ingredients: Propylene glycol: ORAL (LD50): Acute: 20000 mg/kg [Rat]. 22000 mg/kg [Mouse]. DERMAL (LD50): Acute: 20800 mg/kg [Rabbit].

Section 3: Hazards Identification

Potential Acute Health Effects:
Hazardous in case of ingestion. Slightly hazardous in case of skin contact (irritant, permeator), of eye contact (irritant), of inhalation.

Potential Chronic Health Effects:
Slightly hazardous in case of skin contact (sensitizer). CARCINOGENIC EFFECTS: Not available. MUTAGENIC EFFECTS: Not available. TERATOGENIC EFFECTS: Not available. DEVELOPMENTAL TOXICITY: Not available. The substance may be toxic to central nervous system (CNS). 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. Immediately flush eyes with running water for at least 15 minutes, keeping eyelids open. 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:
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.

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: 371°C (699.8°F)

Flash Points: CLOSED CUP: 99°C (210.2°F). OPEN CUP: 107°C (224.6°F) (Cleveland).

Flammable Limits: LOWER: 2.6% UPPER: 12.5%

Products of Combustion: These products are carbon oxides (CO, CO2).

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: 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:
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:
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. 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 oxidizing agents, reducing agents, acids, alkalis, moisture.

Storage:
Hygroscopic. 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:
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. Lab coat. Vapor 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 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 (mg/m3) from AIHA Consult local authorities for acceptable exposure limits.

Section 9: Physical and Chemical Properties

Physical state and appearance: Liquid. (Oily liquid.)

Odor: Practically Odorless.

Taste: Practically Tasteless.

Molecular Weight: 76.1g/mole

Color: Colorless. Clear

pH (1% soln/water): Not available.

Boiling Point: 188°C (370.4°F)

Melting Point: -59°C (-74.2°F)

Critical Temperature: Not available.

Specific Gravity: 1.036 (Water = 1)

Vapor Pressure:
0 kPa (@ 20°C) 0.08 mmHg at 20 C 0.129 mmHg at 25 C

Vapor Density: 2.62 (Air = 1)

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: The product is more soluble in water; log(oil/water) = -0.9

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water, acetone.

Solubility: Soluble in cold water, hot water, acetone.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Incompatible materials, excess heat, exposure to moist air or water

Incompatibility with various substances: Reactive with oxidizing agents, reducing agents, acids, alkalis.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity:
Hygroscopic; keep container tightly closed. Incompatible with chloroformates, strong acids (nitric acid, hydrofluloric acid), caustics, aliphatic amines, isocyanates, strong oxidizers, acid anhydrides, silver nitrate, reducing agents.

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): 18500 mg/kg [Rabbit]. Acute dermal toxicity (LD50): 20800 mg/kg [Rabbit].

Chronic Effects on Humans: May cause damage to the following organs: central nervous system (CNS).

Other Toxic Effects on Humans:
Hazardous in case of ingestion. Slightly hazardous in case of skin contact (irritant, permeator), of inhalation.

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans:
May affect genetic material (mutagenic). May cause adverse reproductive effects and birth defects (teratogenic) based on animal test data.

Special Remarks on other Toxic Effects on Humans:
Acute Potential Health Effects: Skin: May cause mild skin irritation. It may be absorbed through the skin and cause systemic effects similar to those of ingestion. Eyes: May cause mild eye irritation with some immediate, transitory stinging, lacrimation, blepharospasm, and mild transient conjunctival hyperemia. There is no residual discomfort or injury once it is washed away. Inhalation: May cause respiratory tract irritation. Ingestion: It may cause gastrointestinal tract irritation. It may affect behavior/central nervous system(CNS depression, general anesthetic, convulsions, seizures, somnolence, stupor, muscle contraction or spasticity, coma), brain (changes in surface EEG), metabolism, blood (intravascular hemolysis, white blood cells - decreased neutrophil function), respiration (respiratory stimulation, chronic pulmonary edema, cyanosis), cardiovascular system(hypotension, bradycardia, arrhythmias, cardiac arrest), endocrine system (hypoglycemia), urinary system (kidneys), and liver. Chronic Potential Health Effects: Skin: Prolonged or repeated skin contact may cause allergic contact dermatitis. Ingestion: Prolonged or repeated ingestion may cause hyperglycemia and may affect behavior/CNS (symptoms similar to that of acute ingestion). Inhalation: Prolonged or repeated inhalation may affect behavior/CNS (with symptoms similar to ingestion), and spleen

Section 12: Ecological Information

Ecotoxicity:
Ecotoxicity in water (LC50): >5000 mg/l 24 hours [Goldfish]. >10000 mg/l 48 hours [guppy]. >10000 mg/l 48 hours [water flea].

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:

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:
Pennsylvania RTK: Propylene glycol Minnesota: Propylene glycol TSCA 8(b) inventory: Propylene glycol

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):
R21/22- Harmful in contact with skin and if swallowed. S24/25- Avoid contact with skin and eyes.

HMIS (U.S.A.):

Health Hazard: 2

Fire Hazard: 1

Reactivity: 0

Personal Protection: h

National Fire Protection Association (U.S.A.):

Health: 0

Flammability: 1

Reactivity: 0

Specific hazard:

Protective Equipment:
Gloves. Lab coat. Vapor 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 Indutrial Materials. Toronto, Van Nostrand Reinold, 6e ed. 1984. -The Sigma-Aldrich Library of Chemical Safety Data, Edition II. -Supplier MSDS -LOLI -RTECS -HSDB

Other Special Considerations: Not available.

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Last Updated: 05/21/2013 12:00 PM

SAFETY DATA SHEET

Oxygen

Airgas
an Air Liquide company

Section 1. Identification

GHS product identifier : Oxygen

Chemical name : oxygen

Other means of identification : Molecular oxygen; Oxygen molecule; Pure oxygen; O2; UN 1072; Dioxygen; Oxygen USP, Aviator's Breathing Oxygen (ABO)

Product type : Gas.

Product use : Synthetic/Analytical chemistry.

Synonym : Molecular oxygen; Oxygen molecule; Pure oxygen; O2; UN 1072; Dioxygen; Oxygen USP, Aviator's Breathing Oxygen (ABO)

SDS # : 001043

Supplier's details : Airgas USA, LLC and its affiliates
259 North Radnor-Chester Road
Suite 100
Radnor, PA 19087-5283
1-610-687-5253

24-hour telephone : 1-866-734-3438

Section 2. Hazards identification

OSHA/HCS status : This material is considered hazardous by the OSHA Hazard Communication Standard (29 CFR 1910.1200).

Classification of the substance or mixture : OXIDIZING GASES - Category 1
GASES UNDER PRESSURE - Compressed gas

GHS label elements

Hazard pictograms :

Signal word : Danger

Hazard statements : May cause or intensify fire; oxidizer.
Contains gas under pressure; may explode if heated.

Precautionary statements

General : Read and follow all Safety Data Sheets (SDS'S) before use. Read label before use. Keep out of reach of children. If medical advice is needed, have product container or label at hand. Close valve after each use and when empty. Use equipment rated for cylinder pressure. Do not open valve until connected to equipment prepared for use. Use a back flow preventative device in the piping. Use only equipment of compatible materials of construction. Open valve slowly. Use only with equipment cleaned for Oxygen service.

Prevention : Keep away from clothing, incompatible materials and combustible materials. Keep reduction valves, valves and fittings free from oil and grease.

Response : In case of fire: Stop leak if safe to do so.

Storage : Protect from sunlight. Store in a well-ventilated place.

Disposal : Not applicable.

Hazards not otherwise classified : None known.

Section 3. Composition/information on ingredients

Substance/mixture : Substance

Chemical name : oxygen

Other means of identification : Molecular oxygen; Oxygen molecule; Pure oxygen; O2; UN 1072; Dioxygen; Oxygen USP, Aviator's Breathing Oxygen (ABO)

Product code : 001043

CAS number/other identifiers

CAS number : 7782-44-7

Ingredient name	%	CAS number
oxygen	100	7782-44-7

Any concentration shown as a range is to protect confidentiality or is due to batch variation.

There are no 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.

Occupational exposure limits, if available, are listed in Section 8.

Section 4. First aid measures

Description of necessary first aid measures

Eye contact : Immediately flush eyes with plenty of water, occasionally lifting the upper and lower eyelids. Check for and remove any contact lenses. Continue to rinse for at least 10 minutes. Get medical attention.

Inhalation : Remove victim to fresh air and keep at rest in a position comfortable for breathing. 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 adverse health effects persist or are severe. 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. Get medical attention if symptoms occur. Wash clothing before reuse. Clean shoes thoroughly before reuse.

Ingestion : As this product is a gas, refer to the inhalation section.

Most important symptoms/effects, acute and delayed

Potential acute health effects

Eye contact : Contact with rapidly expanding gas may cause burns or frostbite.

Inhalation : No known significant effects or critical hazards.

Skin contact : Contact with rapidly expanding gas may cause burns or frostbite.

Frostbite : Try to warm up the frozen tissues and seek medical attention.

Ingestion : As this product is a gas, refer to the inhalation section.

Over-exposure signs/symptoms

Eye contact : No specific data.

Inhalation : No specific data.

Skin contact : No specific data.

Ingestion : No specific data.

Indication of immediate medical attention and special treatment needed, if necessary

Notes to physician : Treat symptomatically. Contact poison treatment specialist immediately if large quantities have been ingested or inhaled.

Specific treatments : No specific treatment.

Section 4. First aid measures

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 toxicological information (Section 11)

Section 5. Fire-fighting measures

Extinguishing media

Suitable extinguishing media : Use an extinguishing agent suitable for the surrounding fire.

Unsuitable extinguishing media : None known.

Specific hazards arising from the chemical : Contains gas under pressure. Oxidizing material. This material increases the risk of fire and may aid combustion. Contact with combustible material may cause fire. In a fire or if heated, a pressure increase will occur and the container may burst or explode.

Hazardous thermal decomposition products : No specific data.

Special protective actions for fire-fighters : 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. Contact supplier immediately for specialist advice. Move containers from fire area if this can be done without risk. Use water spray to keep fire-exposed containers cool. If involved in fire, shut off flow immediately if it can be done without risk.

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.

Section 6. Accidental release measures

Personal precautions, protective equipment and emergency procedures

For non-emergency personnel : No action shall be taken involving any personal risk or without suitable training. Evacuate surrounding areas. Keep unnecessary and unprotected personnel from entering. Shut off all ignition sources. No flares, smoking or flames in hazard area. Avoid breathing gas. Provide adequate ventilation. Wear appropriate respirator when ventilation is inadequate. Put on appropriate personal protective equipment.

For emergency responders : If specialized clothing is required to deal with the spillage, take note of any information in Section 8 on suitable and unsuitable materials. See also the information in "For non-emergency personnel".

Environmental precautions : Ensure emergency procedures to deal with accidental gas releases are in place to avoid contamination of the environment. Inform the relevant authorities if the product has caused environmental pollution (sewers, waterways, soil or air).

Methods and materials for containment and cleaning up

Small spill : Immediately contact emergency personnel. Stop leak if without risk. Use spark-proof tools and explosion-proof equipment.

Large spill : Immediately contact emergency personnel. Stop leak if without risk. Use spark-proof tools and explosion-proof equipment. Note: see Section 1 for emergency contact information and Section 13 for waste disposal.

Section 7. Handling and storage

Precautions for safe handling

Section 7. Handling and storage

Protective measures : Put on appropriate personal protective equipment (see Section 8). Contains gas under pressure. Avoid breathing gas. Do not puncture or incinerate container. Use equipment rated for cylinder pressure. Close valve after each use and when empty. Protect cylinders from physical damage; do not drag, roll, slide, or drop. Use a suitable hand truck for cylinder movement.

Avoid contact with eyes, skin and clothing. Empty containers retain product residue and can be hazardous. Keep away from clothing, incompatible materials and combustible materials. Keep reduction valves free from grease and oil.

Advice on general occupational hygiene : 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. Remove contaminated clothing and protective equipment before entering eating areas. See also Section 8 for additional information on hygiene measures.

Conditions for safe storage, including any incompatibilities : Store in accordance with local regulations. Store in a segregated and approved area. Store away from direct sunlight in a dry, cool and well-ventilated area, away from incompatible materials (see Section 10). Cylinders should be stored upright, with valve protection cap in place, and firmly secured to prevent falling or being knocked over. Cylinder temperatures should not exceed 52 °C (125 °F). Separate from reducing agents and combustible materials. Store away from grease and oil. Keep container tightly closed and sealed until ready for use. See Section 10 for incompatible materials before handling or use.

Section 8. Exposure controls/personal protection

Control parameters

Occupational exposure limits

Ingredient name	Exposure limits
oxygen	None.

Appropriate engineering controls : Good general ventilation should be sufficient to control worker exposure to airborne contaminants.

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.

Individual protection measures

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.

Eye/face protection : 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. If contact is possible, the following protection should be worn, unless the assessment indicates a higher degree of protection: safety glasses with side-shields.

Skin protection

Hand protection : 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. Considering the parameters specified by the glove manufacturer, check during use that the gloves are still retaining their protective properties. It should be noted that the time to breakthrough for any glove material may be different for different glove manufacturers. In the case of mixtures, consisting of several substances, the protection time of the gloves cannot be accurately estimated.

Section 8. Exposure controls/personal protection

Body protection : 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.

Other skin protection : Appropriate footwear and any additional skin protection measures should be selected based on the task being performed and the risks involved and should be approved by a specialist before handling this product.

Respiratory protection : Based on the hazard and potential for exposure, select a respirator that meets the appropriate standard or certification. Respirators must be used according to a respiratory protection program to ensure proper fitting, training, and other important aspects of use. 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.

Section 9. Physical and chemical properties

Appearance

Physical state : Gas. [Compressed gas.]

Color : Colorless. Blue.

Odor : Odorless.

Odor threshold : Not available.

pH : Not available.

Melting point : -218.4°C (-361.1°F)

Boiling point : -183°C (-297.4°F)

Critical temperature : -118.15°C (-180.7°F)

Flash point : [Product does not sustain combustion.]

Evaporation rate : Not available.

Flammability (solid, gas) : Extremely flammable in the presence of the following materials or conditions: reducing materials, combustible materials and organic materials.

Lower and upper explosive (flammable) limits : Not available.

Vapor pressure : Not available.

Vapor density : 1.1 (Air = 1)

Specific Volume (ft ^{3}/lb) : 12.0482

Gas Density (lb/ft ^{3}) : 0.083

Relative density : Not applicable.

Solubility : Not available.

Solubility in water : Not available.

Partition coefficient: n-octanol/water : 0.65

Auto-ignition temperature : Not available.

Decomposition temperature : Not available.

Viscosity : Not applicable.

Flow time (ISO 2431) : Not available.

Molecular weight : 32 g/mole

Section 10. Stability and reactivity

Reactivity : No specific test data related to reactivity available for this product or its ingredients.

Chemical stability : The product is stable.

Possibility of hazardous reactions : Hazardous reactions or instability may occur under certain conditions of storage or use.
Conditions may include the following:
contact with combustible materials
Reactions may include the following:
risk of causing fire

Section 10. Stability and reactivity

Conditions to avoid : No specific data.

Incompatible materials : Highly reactive or incompatible with the following materials:
combustible materials
reducing materials
grease
oil

Hazardous decomposition products : Under normal conditions of storage and use, hazardous decomposition products should not be produced.

Hazardous polymerization : Under normal conditions of storage and use, hazardous polymerization will not occur.

Section 11. Toxicological information

Information on toxicological effects

Acute toxicity
Not available.

Irritation/Corrosion
Not available.

Sensitization
Not available.

Mutagenicity
Not available.

Carcinogenicity
Not available.

Reproductive toxicity
Not available.

Teratogenicity
Not available.

Specific target organ toxicity (single exposure)
Not available.

Specific target organ toxicity (repeated exposure)
Not available.

Aspiration hazard
Not available.

Information on the likely routes of exposure : Not available.

Potential acute health effects

Eye contact : Contact with rapidly expanding gas may cause burns or frostbite.

Inhalation : No known significant effects or critical hazards.

Skin contact : Contact with rapidly expanding gas may cause burns or frostbite.

Ingestion : As this product is a gas, refer to the inhalation section.

Symptoms related to the physical, chemical and toxicological characteristics

Section 11. Toxicological information

Eye contact : No specific data.

Inhalation : No specific data.

Skin contact : No specific data.

Ingestion : No specific data.

Delayed and immediate effects and also chronic effects from short and long term exposure

Short term exposure

Potential immediate effects : Not available.

Potential delayed effects : Not available.

Long term exposure

Potential immediate effects : Not available.

Potential delayed effects : Not available.

Potential chronic health effects

Not available.

General : 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.

Numerical measures of toxicity

Acute toxicity estimates

Not available.

Section 12. Ecological information

Toxicity

Not available.

Persistence and degradability

Not available.

Bioaccumulative potential

Product/ingredient name	$LogP_{ow}$	BCF	Potential
oxygen	0.65	-	low

Mobility in soil

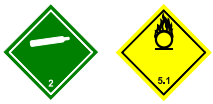
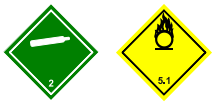
Soil/water partition coefficient (K_{OC}) : Not available.

Other adverse effects : No known significant effects or critical hazards.

Section 13. Disposal considerations

Disposal methods : The generation of waste should be avoided or minimized wherever possible. 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. Dispose of surplus and non-recyclable products via a licensed waste disposal contractor. Waste should not be disposed of untreated to the sewer unless fully compliant with the requirements of all authorities with jurisdiction. Empty Airgas-owned pressure vessels should be returned to Airgas. Waste packaging should be recycled. Incineration or landfill should only be considered when recycling is not feasible. This material and its container must be disposed of in a safe way. Empty containers or liners may retain some product residues. Do not puncture or incinerate container.

Section 14. Transport information

	DOT	TDG	Mexico	IMDG	IATA
UN number	UN1072	UN1072	UN1072	UN1072	UN1072
UN proper shipping name	OXYGEN, COMPRESSED	OXYGEN, COMPRESSED	OXYGEN, COMPRESSED	OXYGEN, COMPRESSED	OXYGEN, COMPRESSED
Transport hazard class(es)	2.2 (5.1) 	2.2 	2.2 (5.1) 	2.2 (5.1) 	2.2 (5.1) 
Packing group	-	-	-	-	-
Environmental hazards	No.	No.	No.	No.	No.

"Refer to CFR 49 (or authority having jurisdiction) to determine the information required for shipment of the product."

Additional information

DOT Classification : **Limited quantity** Yes.
Quantity limitation Passenger aircraft/rail: 75 kg. Cargo aircraft: 150 kg.
Special provisions A52

TDG Classification : Product classified as per the following sections of the Transportation of Dangerous Goods Regulations: 2.13-2.17 (Class 2), 2.23-2.25 (Class 5).
Explosive Limit and Limited Quantity Index 0.125
ERAP Index 3000
Passenger Carrying Ship Index 50
Passenger Carrying Road or Rail Index 75
Special provisions 42

IATA : **Quantity limitation** Passenger and Cargo Aircraft: 75 kg. Cargo Aircraft Only: 150 kg.

Special precautions for user : **Transport within user's premises:** always transport in closed containers that are upright and secure. Ensure that persons transporting the product know what to do in the event of an accident or spillage.

Transport in bulk according to Annex II of MARPOL and the IBC Code : Not available.

Section 15. Regulatory information

U.S. Federal regulations : **TSCA 8(a) CDR Exempt/Partial exemption**: This material is listed or exempted.

Clean Air Act Section 112 (b) Hazardous Air Pollutants (HAPs) : Not listed

Clean Air Act Section 602 Class I Substances : Not listed

Clean Air Act Section 602 Class II Substances : Not listed

DEA List I Chemicals (Precursor Chemicals) : Not listed

DEA List II Chemicals (Essential Chemicals) : Not listed

SARA 302/304

Composition/information on ingredients

No products were found.

SARA 304 RQ : Not applicable.

SARA 311/312

Classification : Refer to Section 2: Hazards Identification of this SDS for classification of substance.

State regulations

Massachusetts : This material is listed.

New York : This material is not listed.

New Jersey : This material is listed.

Pennsylvania : This material is listed.

International regulations

Chemical Weapon Convention List Schedules I, II & III Chemicals

Not listed.

Montreal Protocol (Annexes A, B, C, E)

Not listed.

Stockholm Convention on Persistent Organic Pollutants

Not listed.

Rotterdam Convention on Prior Informed Consent (PIC)

Not listed.

UNECE Aarhus Protocol on POPs and Heavy Metals

Not listed.

Inventory list

Australia : This material is listed or exempted.

Canada : This material is listed or exempted.

China : This material is listed or exempted.

Europe : This material is listed or exempted.

Japan : **Japan inventory (ENCS)**: Not determined.
Japan inventory (ISHL): Not determined.

Malaysia : Not determined.

New Zealand : This material is listed or exempted.

Philippines : This material is listed or exempted.

Republic of Korea : This material is listed or exempted.

Section 15. Regulatory information

Taiwan : This material is listed or exempted.

Thailand : Not determined.

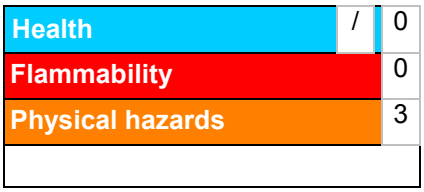
Turkey : Not determined.

United States : This material is listed or exempted.

Viet Nam : Not determined.

Section 16. Other information

Hazardous Material Information System (U.S.A.)



Caution: HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. Although HMIS® ratings and the associated label are not required on SDSs or products leaving a facility under 29 CFR 1910.1200, the preparer may choose to provide them. HMIS® ratings are to be used with a fully implemented HMIS® program. HMIS® is a registered trademark and service mark of the American Coatings Association, Inc.

The customer is responsible for determining the PPE code for this material. For more information on HMIS® Personal Protective Equipment (PPE) codes, consult the HMIS® Implementation Manual.

National Fire Protection Association (U.S.A.)

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Copyright ©2001, National Fire Protection Association, Quincy, MA 02269. This warning system is intended to be interpreted and applied only by properly trained individuals to identify fire, health and reactivity hazards of chemicals. The user is referred to certain limited number of chemicals with recommended classifications in NFPA 49 and NFPA 325, which would be used as a guideline only. Whether the chemicals are classified by NFPA or not, anyone using the 704 systems to classify chemicals does so at their own risk.

Procedure used to derive the classification

Classification	Justification
OXIDIZING GASES - Category 1 GASES UNDER PRESSURE - Compressed gas	Expert judgment According to package

History

Date of printing : 2/3/2018

Date of issue/Date of revision : 2/3/2018

Date of previous issue : 1/27/2017

Version : 0.03

Key to abbreviations : ATE = Acute Toxicity Estimate
BCF = Bioconcentration Factor
GHS = Globally Harmonized System of Classification and Labelling of Chemicals
IATA = International Air Transport Association
IBC = Intermediate Bulk Container
IMDG = International Maritime Dangerous Goods
LogPow = logarithm of the octanol/water partition coefficient
MARPOL = International Convention for the Prevention of Pollution From Ships, 1973

Section 16. Other information

as modified by the Protocol of 1978. ("Marpol" = marine pollution)
UN = United Nations

References : Not available.

Indicates information that has changed from previously issued version.

Notice to reader

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