Allergy Relief at Scale:

Plant Design for Diphenhydramine Hydrochloride

(Technical Report)

Capstone
Presented to the Faculty of the
School of Engineering and Applied Science
University of Virginia

By

Sabrina Liskey, Abigail Janiga, Justin Kim, Vanessa Campbell, Yusra Babar

May 6th, 2025

On our honor as University students, we have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Capstone-Related Assignments.

Signed: *Sabrina Liskey, Abigail Janiga, Justin Kim, Vanessa Campbell, Yusra Babar*

Approved: ______________________________________ Date_________________________
Eric Anderson, Department of Chemical Engineering

Letter of Transmittal

Under the advice of Professor Eric Anderson, we have designed a facility for the manufacture of Diphenhydramine Hydrochloride, an H1 receptor antihistamine medication. The following document has been prepared to communicate the design specifications of the capstone design project.

TABLE OF CONTENTS

I. Summary

Our team has designed a batch manufacturing plant for Diphenhydramine Hydrochloride (DPH-HCl), an H1 receptor antihistamine used for allergy relief. Unlike conventional processes that use bromine, which is corrosive and environmentally hazardous, our plant uses an alternative method using concentrated hydrochloric acid. This innovative approach significantly reduces hazardous byproducts and improves process efficiency while maintaining product purity of 98% or greater. The plant will be located in Ponca City, Oklahoma and will operate 313 days per year with a 24-hour schedule, incorporating eight week-long cleaning periods and two holiday shutdowns. The process is divided into four main blocks: reduction of benzophenone to benzhydrol, chlorination of benzhydrol to chlorodiphenylmethane (CDPM), nucleophilic substitution of CDPM to form DPH, and purification to pharmaceutical quality. Each batch produces 249.46 kg of DPH·HCl. With 1,835 total batches annually, our plant has a production capacity of 457,320 kg per year. We will sell our product for \$3356 per kg. Assuming we sell all of our product, our final net annual profit is \$638 million after taxes and other yearly expenses.

II. Introduction

Diphenhydramine hydrochloride (DPH-HCl) is a well-established and trusted antihistamine used to relieve allergy symptoms. It is often sold as an over-the-counter oral allergy medication. It is a non-addictive, non-toxic medication with minimal harmful side effects. It is primarily used to treat symptoms of allergies (seasonal, food, plant/animal, and bug bites and stings). It has also been used to treat a variety of ailments including Parkinson's disease, motion sickness, insomnia, hay fever, and more. With a current market size of 1.01 billion USD that is anticipated to grow to 1.13 billion USD in the next five years[1], this is a growing and economically profitable industry. Industry experts predict that the global market will grow by about 41% in the next ten years due to expansion into developing regions and an increasing prevalence of allergies caused by urbanization, climate change, and pollution[2]. In addition, cold, flu, and COVID strains have recently started having more chronic and long-term symptoms. The chemical structure for DPH-HCl can be found in Figure 1.

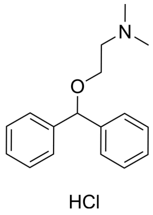


Figure 1. DPH Chemical Structure[3]

Our project explores an alternative to the traditional synthesis that uses bromine. The traditional approach has a 39% atom efficiency in the halogenation step, while our method has a 93% atom efficiency. Therefore, this method considerably reduces hazardous byproducts and improves overall process efficiency. While lab-scale bromine-free methods have successfully created pharmaceutical-grade DPH-HCl, there is little commercial precedent, making our plant design the first of its kind. Our proposed synthesis is the combination of two novel lab-scale methods. The first by Sonavane and Pagire[4] served as the model for the first two reactions and separations. The second by Snead and Jamison[5] was the model for the third reaction and final product purification. The complete synthesis that we explore is depicted in Figure 2.

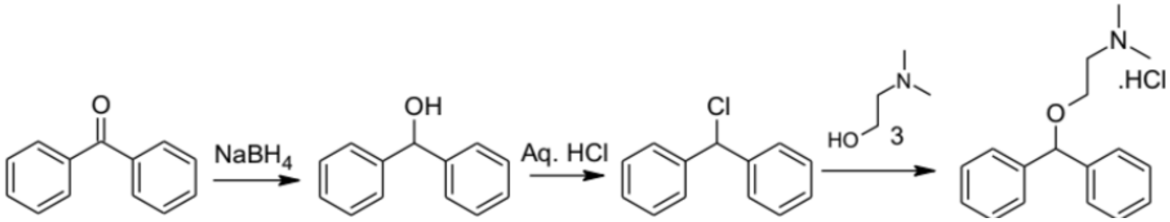


Figure 2. Proposed Synthesis of Diphenhydramine Hydrochloride.[4,5]

Our final product will be sold to a pharmaceutical manufacturing company that will formulate the product into pills or other forms and package and sell it. Our production plant will focus on manufacturing the purified DPH-HCl in Ponca City, Oklahoma. Ponca City is an ideal location due to its existing industrial infrastructure, environment, and low operational costs. The area's history of chemical processing ensures governmental support and reliable utility access. Its remote location also reduces risk to surrounding communities in the event of a hazardous release. The state offers attractive economic incentives like low taxes and cost of living. It also has an extensive trainable, cost-effective workforce and predictable environmental permitting processes.

III. Previous Work

Diphenhydramine hydrochloride (DPH·HCl) was first synthesized by George Rieveschl in 1943. His approach, depicted in Figure 3, utilizes a two-batch process that requires N,N-dimethylaminoethanol, bromodiphenylmethane, a base, and a solvent to create DPH·HCl. Specifically, bromo-diphenylmethane, a key component of Rieveschl's approach, is prepared via the bromination of diphenylmethane. Thus, the usage of bromine causes safety concerns due to its corrosive and toxic nature[6]. Additionally, bromination of diphenylmethane results in a low atom efficiency of 39%, and it requires higher temperatures and residence times for reasonable conversion. The bromination reaction also produces hydrobromide gas, which is a harmful side product that requires careful waste management through very strong alkaline scrubbing systems[4]. Our process will circumnavigate these hazards by removing bromine from the synthesis entirely.

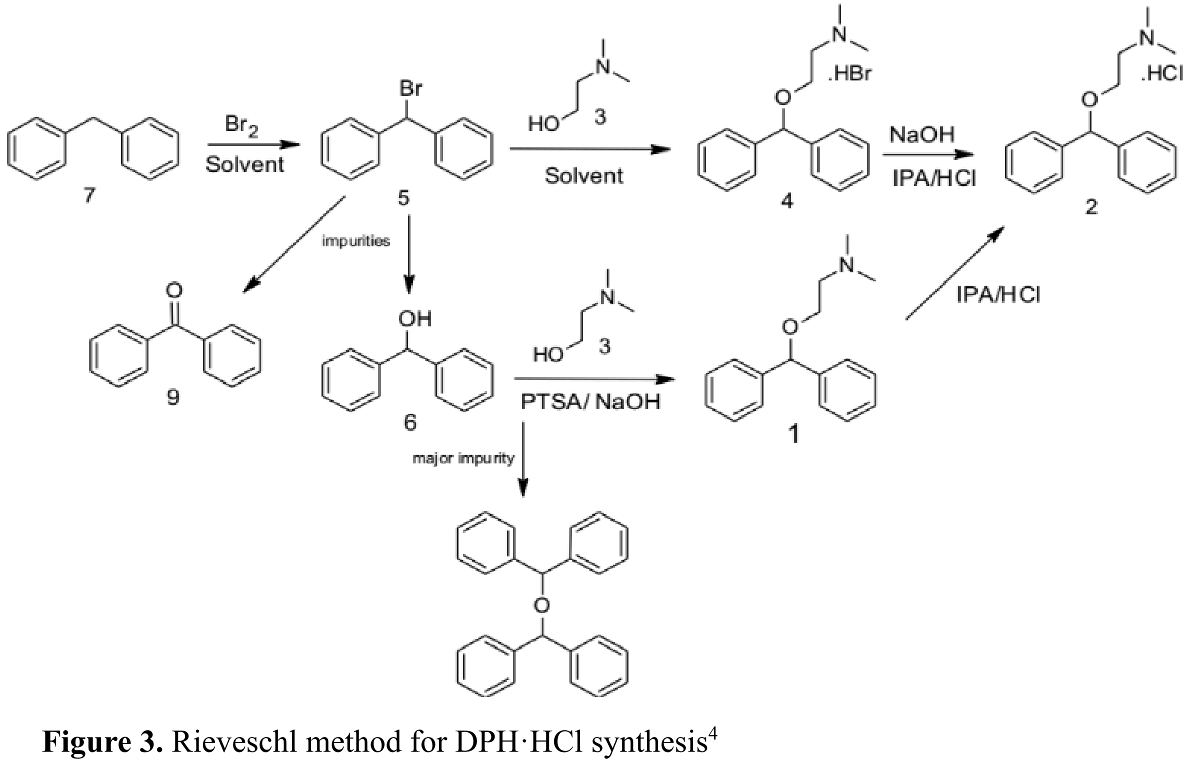


Figure 3. Rieveschl method for DPH·HCl synthesis[4]

IV. Discussion

1. Product specifications

Our target purity of DPH-HCl for oral, over-the-counter (OTC) usage is based on the United States Pharmacopeia (USP) standard, a non-profit organization that establishes standards for the quality, purity, and identity of drugs, food ingredients, and dietary supplements. The USP collaborates with the U.S Food and Drug Administration (FDA) to develop and establish the required standards for OTC oral medications sold in America[7]. The required purity for OTC oral DPH·HCl is no less than 98.0%, calculated on a dry basis.[8] Additionally, certain impurities can also only be present at a certain percentage. For example, the maximum residual benzhydrol and benzophenone quantities are 0.3% each[9]. Our DPH·HCL process creates a product purity of 98%, ensuring that these pharmaceutical standards are met and our product is safe to sell and consume.

For quality assurance, the purity of our product will be quantitatively determined by ^1H NMR spectroscopy using tetramethylsilane (TMS) as an external standard to ensure accurate and reproducible purity assessments for every batch[10]. TMS was chosen because it is a common standard used in NMR since the proton is highly shielded and is attributed a shift of 0 ppm[11].

2. Chemistry

Several chemical reactions take place to convert the starting material, benzophenone, into the final product, DPH·HCl. The first reaction, which occurs in Reactor 1 in Block 1, is the reduction of benzophenone into benzhydrol with reducing agent sodium borohydride. The methanol solvent provides the necessary hydrogen atoms to protonate the alcohol group. The mechanism for this reaction is depicted in Figure 4. Due to the instability of borane, the byproducts of this reaction, $NaOCH_3$ and BH_3, undergo a simultaneous side reaction to produce the final byproducts of the reaction, H_2 and $NaB(OCH_3)_4$[12].

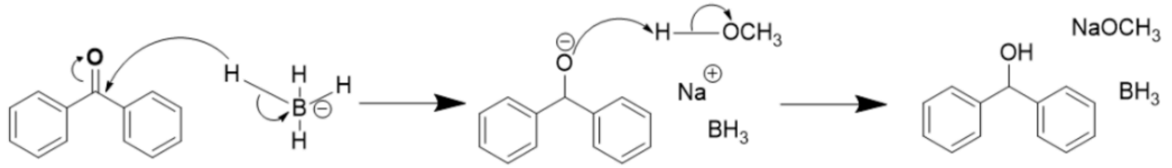


Figure 4. Reaction mechanism for reduction of benzophenone

The second reaction, which occurs in Reactor 2 in Block 2, is the chlorination of benzhydrol with hydrogen chloride (HCl) to produce chlorodiphenylmethane (CDPM). The mechanism for this reaction is depicted in Figure 5.

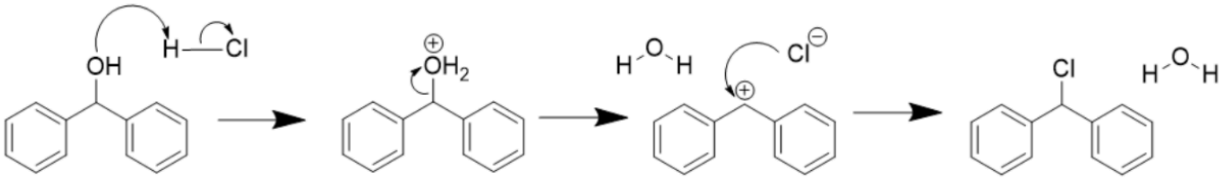


Figure 5. Reaction mechanism for chlorination of Benzhydrol

The third reaction, which occurs in Reactor 3 in Block 3, is a nucleophilic substitution reaction between CDPM and dimethylethanolamine (DMAE) to form diphenhydramine. Throughout blocks 3 and 4, diphenhydramine is converted between its free-base (DPH) and salt (DPH·HCl) forms, which occurs via an acid-base chemical reaction. Both of these mechanisms are depicted in Figure 6. Neutral byproducts are also produced in this reaction and consist of diphenylmethane, 1,1′,2,2′-tetraphenylethane, benzophenone[4].

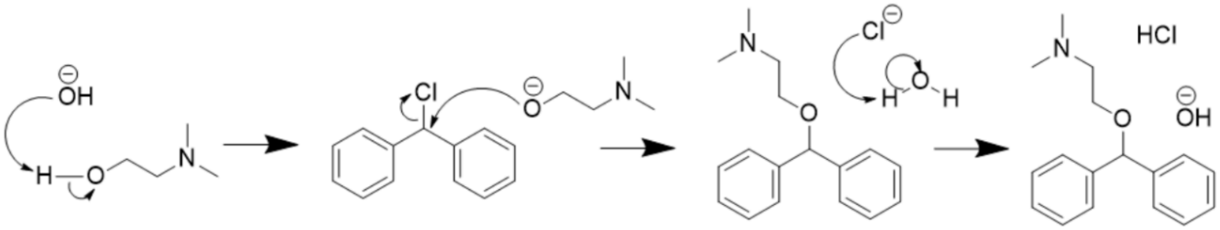


Figure 6. Reaction mechanisms for formation of DPH and DPH·HCl

3. Project Scale Discussion

Our plant scale is determined by the final amount of pure DPH·HCl created per batch and the time required for each batch, which is based on our chosen scale-up from laboratory-scale literature[4,5]. From these metrics, we determined how many batches are possible to complete during designated plant operational hours. While the entire process is primarily batch-based and divided into four blocks, each start-up batch will require 9.87 hours. After that, each block can start immediately after the previous batch finishes. Thus, each subsequent batch requires only 4.066 hours, which is the duration of Block 1, our rate-determining block.

Based on a 24-hour operation schedule with closures for Thanksgiving, New Year's Day and week-long plant cleanings every six weeks that will overlap on Christmas, the plant will close a total of 10 times and operate for 7,512 hours per year. This schedule requires ten 9.87-hour start-up batches per year, totaling 98.7 hours annually. The remaining operational hours of the year produce subsequent batches, which complete every 4.066 hours.

This production schedule yields 1,823 batches per year. Including the start-up batches, the plant will run a total of 1,833 batches annually. Each batch produces 249.46 kg of product, so our plant's final production capacity is 457,320 kg per year, which is approximately 0.75% of the global demand for DPH·HCl in 2023[13].

4. Process Flow Diagram

For organizational purposes, the process is divided into four blocks: reduction of benzophenone to benzhydrol, chlorination of benzhydrol to CDPM, nucleophilic substitution of CDPM to form DPH, and purification. The process flow diagrams for each block are depicted in the sections to follow.

The equipment naming convention is as follows: the letter(s) before the hyphen are an abbreviation for the type of equipment. A legend for these abbreviations is provided in Table 1. The number after the hyphen serves as an identifier for the specific piece of equipment. The first digit indicates the block that the equipment is found in, and the last digit distinguishes equipment of the same type within the same block.

Table 1. Legend for PFD naming conventions

Abbreviation	Meaning
P	Pump
R	Reactor
SF	Screw Feeder
T	Tank
H	Heater
E	Cooler/Condenser
M	Mixer
F	Filter
DR	Dryer
DC	Decanter
C	Crystallizer
B	Blower
CP	Compressor

Block 1

Table 2. Block 1 PFD Legend

Equipment Name	**Description**
P-101	Pumps MeOH from storage into Reactor 1
P-102	Pumps DM water into filter to wash Benzhydrol
P-103	Pumps liquid filtration waste into storage tank for disposal
CP-101	Compresses recycled MeOH and N2 to 15 bar
B-101	Blows air into DR-102
R-101	Reactor 1: Reduction of benzophenone with sodium borohydride and MeOH
SF-101	Feeds benzophenone from storage into Reactor 1
SF-102	Feeds sodium borohydride from storage into Reactor 1
SF-103	Transfers reaction mixture into DR-101
SF-104	Transfers concentrated reaction mixture into the filter
SF-105	Transfers washed reaction mixture from the filter into DR-102
SF-106	Transfers dried reaction mixture from DR-102 into storage
T-101	Methanol storage tank
T-102	Benzophenone storage tank
T-103	Sodium Borohydride storage tank
T-104	DM water storage tank
T-105	Waste tank: DM water with NaB(OCH3)4 and MeOH from block 1 Water, Aq. HCl, unreacted Benzhydrol, residual CDPM from block 2
T-106 (a-d)	N2 storage- 4 tanks each at 25C, 14.8 bar
T-107	Benzhydrol intermediate storage tank
E-101	Condenses and separates methanol from nitrogen for recycle, 15 bar
H-101	Preheats DM water for washing
H-102	Heats Nitrogen for DR-101 to 100C
H-103	Heats air for DR-102 to 120C
F-101	DM water wash and filter
DR-101	Evaporates off methanol to concentrate reaction mass
DR-102	Dries residual water from Benzhydrol

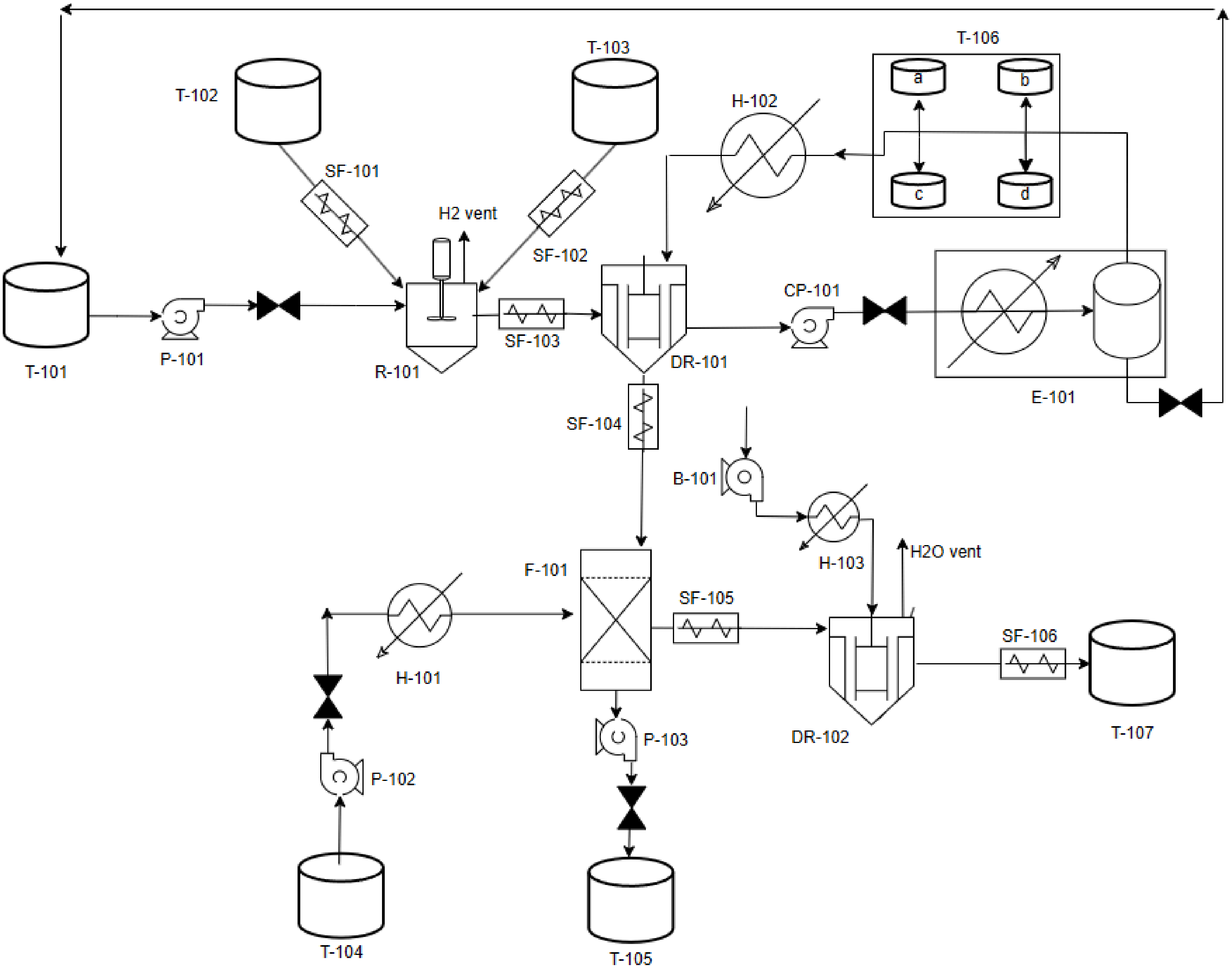


Figure 7. Process Flow Diagram for Block 1 (Reduction of Benzophenone)

Block 2

Table 3. Block 2 PFD Legend

Equipment Name	Description
P-201	Pumps aqueous HCl solution through the heater and into Reactor 2
P-202	Pumps aqueous waste from decanter into waste
R-201	Reactor 2: chlorination of Benzhydrol with HCl
SF-201	Feeds Benzhydrol from storage into Reactor 2
T-107	Benzhydrol intermediate storage tank
T-201	Aqueous HCl storage tank
T-202	CDPM intermediate storage tank
H-201	Preheats aqueous HCl solution
DC-201	Separates waste water stream and CDPM stream

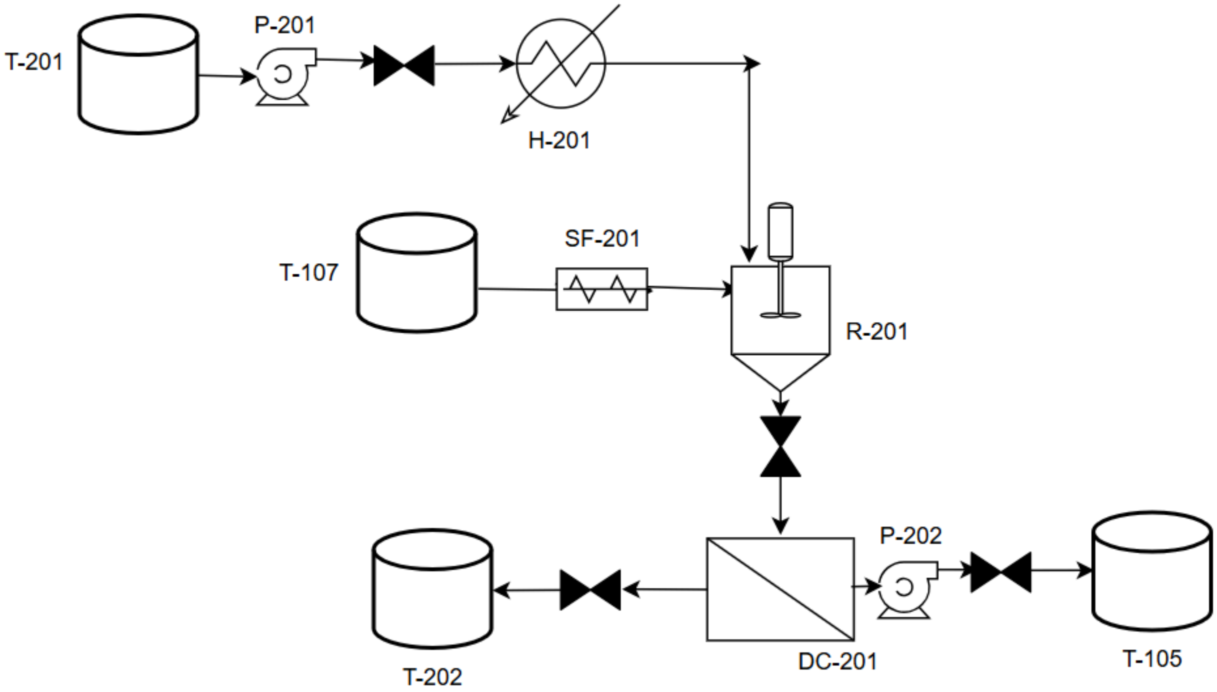


Figure 8. Process Flow Diagram for Block 2 (Chlorination of Benzhydrol)

Block 3

Table 4. Block 3 PFD Legend

Equipment Name	Description
P-301	Pumps liquid CDPM into Reactor 3
P-302	Pumps liquid DMAE from storage into Reactor 3
P-303	Pumps reaction mixture into M-301
P-304	Pumps Aq. NaOH solution through the heater and into the mixer
R-301	Reactor 3: Nucleophilic substitution of CDPM with DMAE
T-202	Heated CDPM intermediate storage tank
T-301	DMAE storage tank
T-302	Aq. NaOH storage tank
T-303	Unpurified DPH intermediate storage tank
H-301	Preheats Aq. NaOH
E-301	Cools unpurified DPH to ambient temperature and pressure
M-301	Mixes reaction mixture with Aq. NaOH

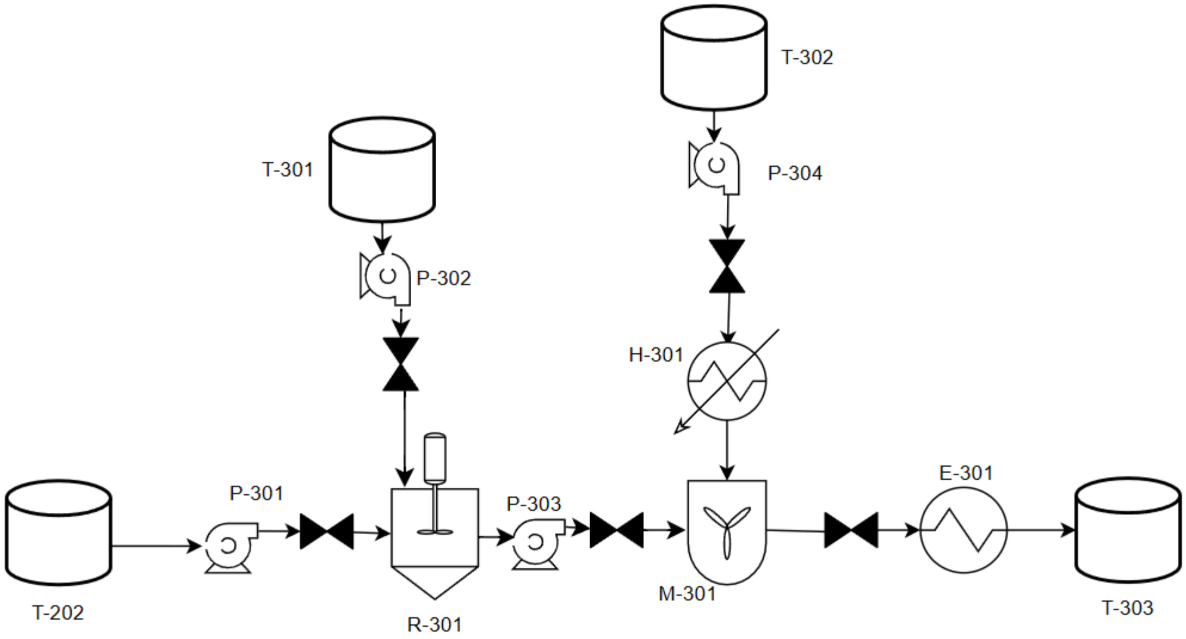


Figure 9. Process Flow Diagram for Block 3 (Nucleophilic Substitution of CDPM)

Block 4

Table 5. Block 4 PFD Legend

Equipment Name	Description
P-401	Pumps neutralized DPH from storage into the decanter
P-402	Pumps hexane from storage into the decanter
P-403	Pumps DPH salt dissolved in liquid hexane from decanter into crystallizer
P-404	Pumps liquid hexane from storage into the filter
P-405	Pumps liquid 5M HCl/IPA solution into the crystallizer
P-406	Pumps liquid filtration waste into storage tank
P-407	Pumps hexane from storage into the crystallizer
CP-401	Compresses vaporized hexane and N2 to 20 bar
SF-401	Recycles filtered DPH from the filter back into the crystallizer
SF-402	Transfers the washed DPH from the filter into the dryer
SF-403	Transfers the dried DPH from the dryer into the final product storage
T-303	Unpurified DPH intermediate storage tank
T-401	Hexane storage tank
T-402	5M HCl/IPA storage tank
T-403	Decanter aqueous waste storage tank
T-404	Filter solvent waste: HCl, IPA, hexane, trace impurities
T-405 (a-d)	N2 Storage tanks- 4 tanks, 25C and 14.6 bar
T-406	Final DPH-HCl product storage
E-401	Condenses and separates hexane from nitrogen for recycle, 20 bar
H-401	Heats N2 for DR-401 to 100C
F-401	Hexane wash and filter
DR-401	Dries residual solvent from final product
DC-401	Separates free base DPH in hexane and DPH salt
C-401	Crystallizes DPH salt

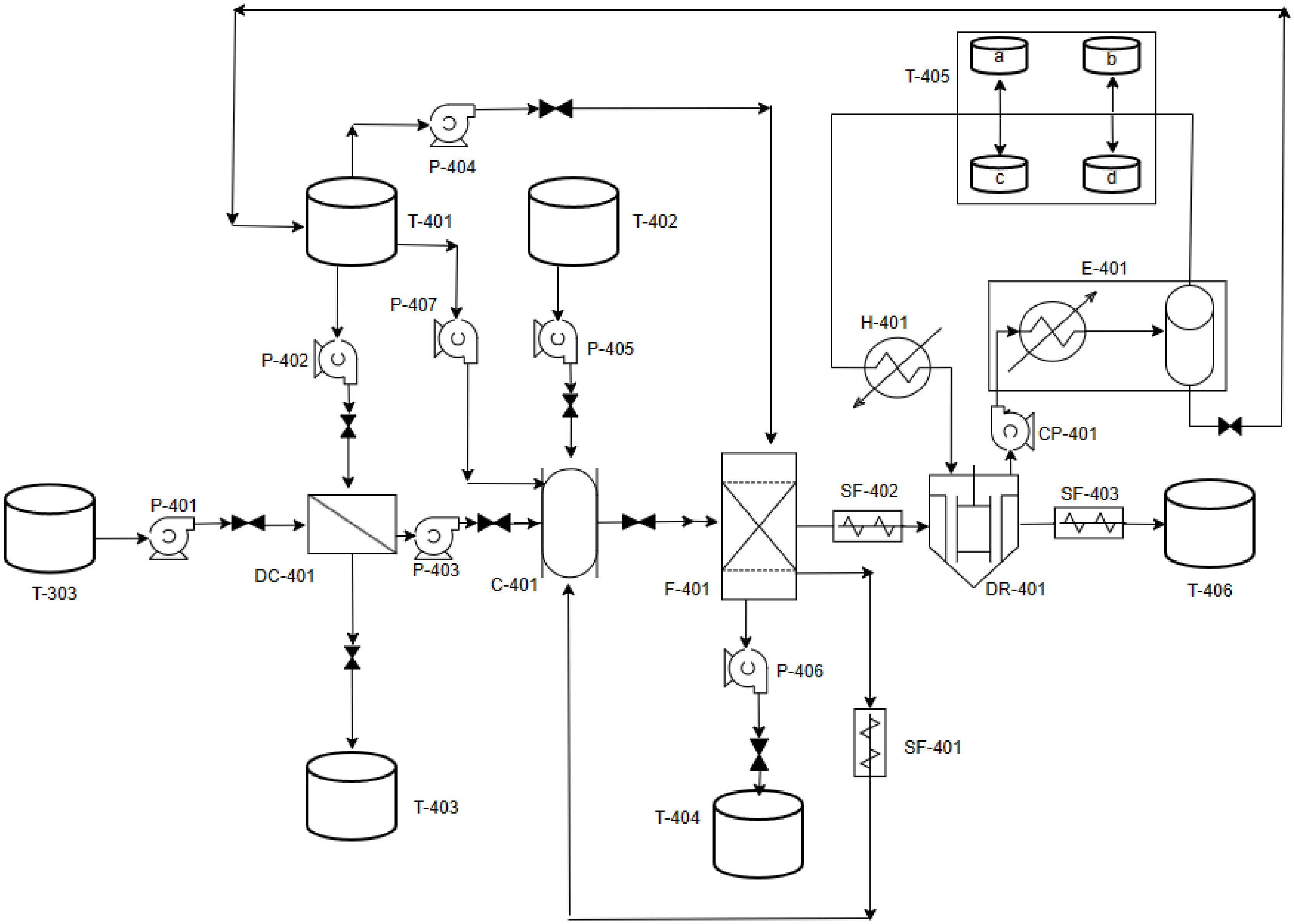


Figure 10. Process Flow Diagram for Block 4 (Purification of DPH)

5. Equipment Design Discussion

The plant will use a centralized cooling system that contains all house utilities. The heating utilities continuously supplied on site will include 5 and 15 bar steam. Chilled water will be supplied at 10°C, and cooling water will be supplied at 27°C. The cooling utilities continuously supplied on site will include glycol at -30°C and -5°C.

Batch Reactors

Reactor 1 (R-101): Reduction of Benzophenone

Reactor 1 produces benzhydrol, which is the reduced alcohol form of benzophenone. To begin, 225.0 kg of benzophenone is fed as a solid into an 800 L batch reactor constructed of A316 stainless steel. Then, 356.9 kg of methanol is added and mixed with the benzophenone until dissolved. After mixing, 44.8 kg sodium borohydride is fed to create a liquid solution with a total volume of 702.45 L. The reactor has a height of 1.6 m and a diameter of 0.8 m. The reaction is mixed using a marine impeller (chosen for its suitability in low-viscosity systems and low power usage) that is 0.26 m in diameter and 0.53 m above the bottom of the reactor. The mixture density was determined using Eq R.2. The impeller will rotate at 240 rev/min to ensure turbulent flow ($Re \approx 10{,}000$), requiring 29.3 W of power. Power requirements for the impeller were determined using Eq R.4. Detailed R-101 impeller power calculations can be found in the Appendix. The reactor has a residence time of 2 hours to achieve full conversion of sodium borohydride. The reactor was modeled in Aspen Plus v14 using an RBatch block with a 27°C operating temperature and a 1 bar operating pressure. The reaction rate is estimated to be 18700 mol/s with an activation energy of 56.9 kJ/mol using Eq R.1. Our reaction takes place in methanol because it was used in our synthesis source (Sonavane and Pagire[3]); however, the experimental kinetic data used to simulate reaction 1 was performed in isopropyl alcohol (IPA)[14]. There is no publicly available kinetic data for this reaction in methanol. We predict that our reaction in methanol will have a faster rate than the estimation used in IPA given methanol's higher polarity, smaller particle size, and lower viscosity. Determining more accurate reaction kinetics would require additional experimentation. Hydrogen gas is also produced at 7.16 kg/h via a side reaction. The heat duty generated by the reaction is -61.7 kW for each batch. The mixture's heat capacity, viscosity, and thermal conductivity were estimated using Aspen Plus v14's property databanks. These values can be found in the Appendix. Thermal conductivity of the mixture is 0.196 W/m-K and the heat transfer coefficient is 122.65 W/m^2-K. The mixture's heat transfer coefficient was determined by Eq R.5 with a Reynolds number of 10,000, and cooling fluid mass was determined using Eq R.7. Due to the exothermic nature of the reaction, a coil with propylene glycol at -30°C and 1643.4 kg/h is used to maintain a reactor operating temperature of 27°C. A coil was chosen over a jacketed reactor as the required cooling surface area was larger than the tank's surface area. -30°C glycol was chosen because it is part of the plant's centralized cooling system and provides a large enough temperature differential for adequate cooling without an excessive flow rate or coil size. The coil has a diameter of 2 cm and a cooling surface area of 8.82 m^2. The coil is 0.56 m tall. Coil dimensions were determined using Eq R.6. Detailed R-101 heat transfer calculations can be found in the Appendix. Reactor dimensions can be found in Table 6. After exiting R-101, the wet, solid product will move forward within the synthesis process.

Reactor 2 (R-201): Chlorination of Benzhydrol

Reactor 2 facilitates the chlorination reaction of benzhydrol with hydrogen chloride to produce chlorodiphenylmethane (CDPM). To begin, 463.6 kg of a 37% aqueous HCl solution is fed with 200 kg of solid benzhydrol powder into a batch reactor, resulting in a liquid with a total volume of 612 L. The reaction takes place in a 700 L batch reactor constructed from Hastelloy, a nickel alloy resistant to corrosion from HCl. The reactor has a height of 1.52 m and a diameter of 0.76 m. Mixing is achieved using a marine impeller (chosen for its suitability in low-viscosity systems and low power usage) with a diameter of 0.25 m, positioned 0.51 m above the bottom of the reactor. The mixture density was determined using Eq R.2. The impeller will rotate at 240 rev/min to ensure turbulent flow ($Re \approx 10{,}000$), requiring 29 W of power. Power requirements for the impeller were determined using Eq R.4. Detailed R-201 impeller power calculations can be found in the Appendix. The reactor has a residence time of 2 hours to achieve a full conversion of benzhydrol. The reactor was modeled in Aspen Plus v14 using an RBatch block at an operating temperature of 83°C and a pressure of 15 bar. The reaction rate was estimated using

Eq R.1 to be 0.00774 s^{-1} with an activation energy of 10 kJ/mol. To stay consistent with the procedure from Sonavane and Pagire[3], our second reaction does not use a solvent. However, the experimental kinetic data used to simulate reaction 2 was performed in toluene[15]. There is no publicly available kinetic data for this reaction without a solvent. Determining more accurate reaction kinetics would require additional experimentation. The heat duty generated by the reaction is -93.91 kW per batch, with an overall heat transfer coefficient of 158.4 W/m^2-K. A coil with chilled water at 10°C flowing at 1106.30 kg/h will maintain the reactor temperature at 83°C. A coil was chosen over a jacketed reactor as the required cooling surface area was larger than the tank's surface area. The mixture's heat transfer coefficient was determined by Eq R.5 with a Reynolds number of 10,000 and cooling fluid mass was determined using Eq R.7. The mixture's heat capacity, viscosity, and thermal conductivity were estimated using Aspen Plus v14's property databanks. The coil has a diameter of 2 cm, a cooling surface area of 7.72 m^2, and a height of 0.514 m. Coil dimensions were determined using Eq R.6. Detailed heat transfer calculations can be found in the Appendix. Reactor dimensions can be found in Table 6. After exiting R-201, the two phase liquid-liquid mixture will move forward within the synthesis process.

Reactor 3 (R-301): Synthesize Hydrochloride Salt of Diphenhydramine

Reactor 3 facilitates the formation of the hydrochloride salt of DPH. To begin, 220.02 kg of liquid CDPM and 101.46 kg of liquid dimethylethanolamine (DMAE) are fed into a 400 L batch reactor constructed from A316 stainless steel. The reactor has a height of 1.24 m and a diameter of 0.6 m. The reaction will have a residence time of 1.2 hours and an operating temperature and pressure of 175°C and 17.24 bar. Mixing is achieved using a marine impeller (chosen for its suitability in low-viscosity systems and low power usage) with a diameter of 0.21 m, positioned 0.413 m above the reactor floor. The impeller will rotate at 240 rev/min to ensure turbulent flow ($Re \approx 10{,}000$), requiring 13 W of power. Power requirements for the impeller were determined using Eq R.4. The mixture density was determined using Eq R.2. Detailed R-301 impeller power calculations can be found in the Appendix. The reaction was simulated in Aspen Plus v14 using an RSTOIC block. A 100% conversion of CDPM was assumed due to limited data; although, in practice, a small amount of unreacted material may remain. This endothermic reaction requires 38.94 kW of heat duty to maintain a temperature of 175°C. A steam coil is utilized with an overall heat transfer coefficient of 308.8 W/m^2-K. The mixture's heat capacity, viscosity, and thermal conductivity were estimated using Aspen Plus v14's property databanks. A coil was chosen over a jacketed reactor as the required heating surface area was larger than the tank's surface area. The mixture's heat transfer coefficient was determined by Eq R.5 with a Reynolds number of 10,000, and the steam flow rate was determined using Eq R.7. The coil has a diameter of 2 cm, a heating surface area of 5.48 m^2, and a height of 0.45 m. Saturated steam at 15 bar (198°C) is supplied at a rate of 147.89 kg/h. The steam condenses and exits the coil as a liquid at 175°C and 10 bar[16]. The fluid will exit at 175°C, as it is the temperature of the reaction. Coil dimensions were determined using Eq R.6. Detailed heat transfer calculations can be found in the Appendix. The resulting product is a liquid-liquid mixture that will exit the reactor and move forward within the synthesis process.

Table 6. Summary of reactor designs

	R-101	**R-201**	**R-301**
Residence Time (h)	2	2	1.2
Liquid (L)	702.5	612	374.3
Tank Volume (L)	800	700	400
Tank Height (m)	1.6	1.52	1.24
Tank Diameter (m)	0.8	0.76	0.62
Impeller Height from Base (m)	0.53	0.507	0.413
Impeller Diameter (m)	0.26	0.253	0.21
Baffle Dimensions (4x) (m)	0.08 x 0.08	0.076 x 0.076	0.062 x 0.062

Reactor Design Equations

Power calculations assume a power number of 0.5. Important design equations are as follows:

Reaction Expression Arrhenius equation

k = rate constant (mol/s)
E_a= activation energy (kJ/mol)
R = Gas Constant (kJ/K-mol)
T = Temperature (K)
A = Frequency Factor

$$k = Ae^{(-E_a/RT)} \qquad \text{Eq R.1}$$

Mixture Density

$$\rho = \frac{M_{total}}{V_{total}} \qquad \text{Eq. R.2}$$

Impeller Power

N= rotations/min
rps = rotations/sec
d = tank diameter
D = diameter of impeller (m)
ρ = density of fluid
μ = viscosity of fluid
N_p = propeller type value
P = Impeller power

$$Re = \frac{N\, d^2\, \rho}{\mu} \qquad \text{Eq R.3}$$

$$P = N_p\, \rho\, (\text{rps})^3\, D^5 \qquad \text{Eq R.4}$$

Mixing and Heat Transfer with Coil[17]

h = Heat transfer coefficient for mixture
k = thermal conductivity of mixture
μ_j/μ = viscosity at wall surface/ viscosity of mixture = assume 1
Re = Reynolds number
C_p = mixture heat capacity
Q = heat duty

U = Overall heat transfer coefficient = assume equal to hj
A = surface area
D = Tank Diameter
T_{mix} = reaction temperature
T_{cool} = temperature of cooling fluid
$\dot{m}$ = fluid mass flow rate

$$\frac{\frac{hD}{k}\left(\frac{\mu_j}{\mu}\right)^{0.14}}{\left(\frac{C_p\mu}{k}\right)^{1/3}} = 0.87Re^{0.62} \qquad \text{Eq R.5}$$

$$Q = UA\left(T_{mix} - T_{cool}\right) \qquad \text{Eq R.6}$$

$$Q = \dot{m}C_p dt \qquad \text{Eq R.7}$$

Rotary Dryers

All dryers are rotary dryers with a 2° angle to allow the solids to rotate down the dryer. The dryers were modeled in Aspen Plus v14 using a Flash Block with their respective liquids to be evaporated. All dryers operate at atmospheric pressure. DR-101 and DR- 401 use nitrogen gas, while DR-102 uses air. Detailed calculations for each rotary dryer can be found in the Appendix. The heat capacity of each mixture was estimated using Eq D.1. The total heat generated or consumed was determined using Eq. D.2, D.3, D.4, D.5, and D.6. The heat transfer coefficient for the dryer was determined using Eq. D.7, with an assumed mass velocity of 515 kg/h-m^2 for each gas[18]. This value was assumed based on the combination of the root mean square velocity of air and nitrogen and the Handbook of Industrial Drying, but further experimentation would be required for a mass velocity specific to our materials. The dryer length was determined by Eq D.8. The final drying time was determined by Eq D.9 with an assumed particle diameter of 4000 µm for each material based on literature standards[18].

Dryer (DR-101)

The slurry product from Reactor 1 enters DR-101 to concentrate the product stream by evaporating off methanol. The product stream enters the dryer at 33.1 wt% methanol and is dried to about 5%. The total feed is 619.5 kg. This dryer has a diameter of 2.43 m, a length of 14.82 m, operating at 1 bar and a rotational speed of 3.92 RPM. Because methanol is volatile, nitrogen flows at 2400 kg/h at 100°C to heat the product to 68°C—above methanol's 64.7°C boiling point. At atmospheric pressure, benzhydrol, benzophenone, and sodium tetramethoxyborate have melting points of 69°C, 119°C, and 255°C, respectively. Thus, the temperature of the product will be lower than these melting points to avoid melting the solids. One precaution to consider is that benzhydrol may become malleable this close to its melting point. Drying takes 16.44 minutes and was found using equation D.9. Methanol-saturated nitrogen exits at 69.74°C, while the dried solids (435.17 kg) leave at 68°C. Total vapor outflow is 2789.84 kg/h, which is transferred to a condenser to extract the methanol from the nitrogen for recycle.

Dryer (DR-102)

The wet, solid product from F-101 enters DR-102 to evaporate off excess water. There is no residual methanol from the previous wash and filter step. The product starts at 33.3% water and is dried to about 1%. This dryer has a diameter of 2.74 m, a length of 29.65 m, and a rotational speed of 3.49 RPM. Air flows at 2938.70 kg/h at 120°C to heat the product to 68°C—below water's 100 °C boiling point. Benzhydrol has melting points of 69°C, so one precaution to consider is that benzhydrol may become malleable if it is near its melting point. Drying takes 28.32 minutes and was found using equation D.9. Water- saturated air exits at 102.71°C, and the dried solids (200 kg) leave at 68°C. Total vapor outflow is 3109.1 kg/h, which is vented to the atmosphere.

Dryer (DR-401)

The total feed is 371.86 kg. This dryer has a diameter of 2.02 m, a length of 9.62 m, and a rotational speed of 4.71 RPM. Nitrogen flows at 1660.41 kg/h at 100°C to heat the product to 70°C—above hexane's 68.7°C boiling point. At atmospheric pressure, DPH has a melting point of 166°C, so the temperature of the product will be lower to avoid melting the solid. Drying takes 10.64 minutes. Hexane-saturated nitrogen exits at 87.59°C, while the dried solids (249.46 kg) leave at 70°C. Total vapor outflow is 2122.4 kg/h. which is transferred to a condenser to extract the hexane from the nitrogen for recycle.

Heat Capacity of Each Mixture

m = mass of solid

c = specific heat of solid

$$Cp_{\text{mixture}} = \frac{\sum_{i=1}^{n} m_i \, c_i}{\sum_{i=1}^{n} m_i} \quad \text{Eq D.1}$$

Heat to Dry Solid from Inlet Temperature to Final Temperature

Q_1 = the rate of heat transfer

$\dot{m}$= total mass flow rate

$C_{p,solid}$ = specific heat of solid

$$Q_1 = \dot{m}C_{P,solid}(T_{final} - T_{Initial}) \quad \text{Eq D.2}$$

Heating Moisture to Vaporization Temperature

Q_2 = the rate of heat transfer

$\dot{m}$ = total mass flow rate

$C_{p,\ moisture}$ = specific heat of solvent

$$Q_2 = \dot{m}C_{p,moisture}(T_{vap} - T_{initial}) \quad \text{Eq D.3}$$

Heat to Evaporate Moisture

Q_3 = the rate of heat transfer

$\dot{m}$ = mass % of moisture * total flow rate

$h_{vap,moisture}$ = heat of vaporization of liquid

$$Q_3 = \dot{m}h_{vap,moisture} \quad \text{Eq D.4}$$

Heat Residual Moisture to Final Temperature

Q_4 = the rate of heat transfer
$\dot{m}_{total}$ = total mass flow rate
$C_{p,solid}$ = specific heat of solid

$$Q_4 = \dot{m}_{total} * 0.01 C_{p,solid}(T_{final} - T_{initial}) \quad \text{Eq D.5}$$

Total Heat Consumed (assuming 10% of heat generated is lost to surroundings)

$$Q_{Total} = 0.9 * (Q_1 + Q_2 + Q_3 + Q_4) \quad \text{Eq D.6}$$

Heat Transfer Coefficient

G = gas mass velocity (assumed to be 515 kg/h-m^2 for each gas)[18]
D = diameter of dryer

$$U_a = 4\, G^{0.67}\, \frac{1}{D} \quad \text{Eq D.7}$$

Dryer Length

t_{lm} = logarithmic mean temperature difference
U_a = heat transfer coefficient
Q = rate of heat transfer
d = diameter of dryer

$$L = \frac{4\,Q}{\pi\, d^2\, U_a\, t_{\text{lm}}} \quad \text{Eq D.8}$$

Total Drying Time[18]

S = dryer angle of 2°
N = the dryer RPM
B = particle diameter (assumed to be 4000 µm for each material)
L = dryer length
G = Gas Mass Velocity
D = dryer diameter
m = mass flow rate

$$\tau = \frac{0.3344\,L}{S\,N^{0.9}\,D} + \frac{0.608\,BLG}{m_{\text{feed}}} \qquad \text{Eq D.9}$$

Heat Exchangers

All heaters are countercurrent, shell-and-tube heat exchangers modeled in Aspen Plus v14 with a HeatX block. They use saturated steam as the heat transfer fluid. The exchangers are designed with different materials and operating pressures to suit each fluid, and the appropriate property methods (Peng-Robinson, NRTL, or Elec-NRTL) are used to capture fluid behavior.

Heater (H-101)

Heater H-101 preheats demineralized (DM) water to 60°C for the water wash step. The heater handles all three 800 L washes (a total of 2400 L) at once since the washes will occur in quick succession and so the water will not need to be held at high temperature. It was modeled in Aspen with NRTL as the property method. Heating requires 98 kW of power. The exchanger is made of stainless steel with water in the shell and uses 5 bar saturated steam (153 kg/h) in the tubes, which condenses to water at 5 bar and 112°C. A minimum heat transfer surface area of 1.1 m^2 is required.

Heater (H-102)

Heater H-102 preheats 2400 kg/h of nitrogen to 100°C to enter the methanol recovery dryer (DR-101). It was modeled with the Peng-Robinson equation of state in Aspen Plus v14. Heating requires 1.44 m^2 of surface area for heat transfer and 52.1 kW of power. The heat transfer fluid is 15 bar saturated steam at 250 kg/hr, which condenses to water at 15 bar and 38°C. The exchanger keeps the steam in the tubes.

Heater (H-103)

Heater H-103 preheats 2938.70 kg/h of air to 120°C to enter the benzhydrol dryer (DR-102). It was modeled with the Peng-Robinson equation of state in Aspen Plus v14. Heating requires 2.00 m^2 of surface area for heat transfer and 78.0 kW of power. The heat transfer fluid is 15 bar saturated steam at 400 kg/hr, which condenses to water at 15 bar and 49°C. The exchanger keeps the steam in the tubes.

Heater (H-201)

Heater H-201 preheats 580 L of 15 bar aqueous HCl reactor feed to 83°C. It was modeled with Elec-NRTL and the electrolyte wizard, which accounts for HCl dissociation. The process requires 33.9 kW of power and uses a Hastelloy exchanger running at 15 bar (keeping the fluid liquid) with the aqueous HCl in the tubes. Here, 5 bar saturated steam enters at 54 kg/h and condenses to water at 5 bar and 122°C. The required heat transfer surface area is 0.42 m^2.

Heater (H-301)

Heater H-301 preheats 809 L of aqueous 3M NaOH to 175°C for neutralizing protonated amines (with NaOH added at a 4:1 ratio to Reactor 3 effluent at 17 bar)[5]. Modeled with Elec-NRTL and the electrolyte wizard, heating requires 145 kW. Because NaOH is corrosive to stainless steel at high temperatures, a Nickel 200[19] exchanger is used, operating at 17 bar. In this exchanger, 15 bar saturated steam enters at 234 kg/h and condenses to water at 15 bar and 147°C. A minimum of 2.3 m^2 of heat transfer surface area is needed.

Cooler (E-301)

Cooler E-301 cools neutralized reactor effluent from 175°C to 25°C for storage. It was modeled in Aspen using a HeatX block with NRTL as the property method and requires 169 kW of power. A Nickel 200 countercurrent shell-and-tube heat exchanger operating at 17 bar handles the corrosive mixture (with unreacted NaOH inside the Nickel tubes). Glycol at –30°C flows through the shell at 4655 kg/h and exits at 19°C, providing the high temperature driving force needed. The exchanger requires a minimum of 2.5 m^2 of heat transfer surface area.

Heater (H-401)

Heater H-401 preheats 1660.41 kg/h of nitrogen to 100°C to enter the final product dryer (DR-101). It was modeled with the Peng-Robinson equation of state in Aspen Plus v14. Heating requires 0.95 m^2 of surface area for heat transfer and 36 kW of power. The heat transfer fluid is 15 bar saturated steam at 175 kg/hr, which condenses to water at 15 bar and 40°C. The exchanger keeps the steam in the tubes.

The condensers were modeled in Aspen Plus v14 using a HeatX block and use Hastelloy countercurrent shell-and-tube heat exchangers. They cool saturated nitrogen gas to condense the volatile component (methanol or hexane) from the nitrogen mixture. In each condenser, the corrosive mixture is contained within the tubes, while glycol serves as the heat transfer fluid in the shell. After cooling, the liquid–vapor mixture is flashed for complete phase separation. Although we assume perfect separation, very small amounts of the volatile component may still be in the nitrogen gas, which will evaporate out in subsequent cycles.

Condenser and Vapor-Liquid Separation (E-101)

Condenser E-101 cools 2789.84 kg of methanol-saturated nitrogen gas feed to a temperature of 27°C. Cooling this mixture requires 48.92 kW of power. The heat transfer fluid is glycol at -30°C that enters the heat exchanger shell at 3500 kg/h and exits at -8.20°C. This exchange requires a minimum of 0.83 m^2 of available surface area for heat transfer.

The vapor-liquid mixture is then flashed through a vapor-liquid separator to fully separate the methanol from the nitrogen gas. This vapor-liquid separator operates at 15 bar and 27°C, which was found using an Aspen Plus v14 Flash2 module. The nitrogen gas is then transferred to the nitrogen storage tank at 14.8 bar, and the methanol is transferred to the methanol liquid storage tank at 1 bar.

Condenser and Vapor-Liquid Separation (E-401)

Condenser E-401 cools 2124.73 kg of hexane-saturated nitrogen gas feed to a temperature of 27°C. Cooling this mixture requires 52.32 kW of power. The heat transfer fluid is glycol at -30°C that enters the heat exchanger shell at 1000 kg/h and exits at 22°C. This exchange requires a minimum of 0.54 m^2 of available surface area for heat transfer.

The vapor-liquid mixture is then flashed through a vapor-liquid separator to fully separate the hexane from the nitrogen gas. This vapor-liquid separator operates at 20 bar and 27°C, which was found using an Aspen Plus v14 Flash2 module. Then, the nitrogen gas is transferred to the nitrogen storage tank at 14.7 bar, and the hexane is transferred to the hexane liquid storage tank at 1 bar.

Mixers and Separators

Wash and Filter (F-101)

To wash the output from DR-101, a three-wash sequence is performed using 800 L of preheated demineralized water[4] per wash (twice the volume of the solid mass) following industry standards. Benzophenone is sparingly soluble in water, so any residual amount in the benzhydrol product is assumed to be negligible. The water is first warmed to 60°C to improve the dissolution of methanol and borate salts. A 20 wt% solubility for $NaB(OCH_3)_4$ in water was assumed due to limited published data and the generally high solubility of ionic sodium borate salts at this temperature[8]. The filter was designed with a volume of 3 m^3, a diameter of 1.96 m, and a height of 3.92 m. Filter calculations can be found in the Appendix. Wet, solid benzhydrol proceeds to a dryer, while the water and byproduct stream—containing the remaining benzophenone, methanol, and borate salts—is stored in a waste tank for treatment. The estimated time of processing is 1.32 h.

Wash and Filter (F-401)

For final washing of the crystallizer output, a two-wash sequence is performed using 400 L of hexane per wash (800 L total). Due to hexane's nonpolar nature, free-base DPH dissolves selectively, allowing isolation of the pure solid DPH·HCl salt as the byproducts remain in the liquid phase. The hexane is maintained at 25°C to ensure proper phase separation. Wet solid DPH·HCl moves forward to the final dryer, while the hexane and byproduct stream is stored in a waste tank for treatment. The filter is designed with a volume of 2.5 m^3, a diameter of 1.85 m, and a height of 3.7 m. The product will then be recycled through the crystallizer and back to the filter for the second wash. The estimated time for each pass through of F-401 is 29.76 minutes, which totals to 59.52 minutes for both passes through the F-401.

Filter calculations can be found in the Appendix. For both filters F-101 and F-401, future design work would be needed to determine the detailed filter design such as membrane type, pore size, and vacuum pressure.

All decanters are horizontal, batch, cylindrical vessels designed to separate phases based on density differences. Each decanter includes a 15% buffer over the calculated liquid volume to ensure sufficient residence time for settling. The settling velocity design equation (Eq. DC.1) was used to determine residence time for each decanter. Calculations for each decanter can be found in the Appendix.

Batch Decanter (DC-201)

DC-201 receives 663.6 kg of R-201 output with mass fractions of 0.1988 HCl, 0.332 CDPM, and 0.47 water. It separates the aqueous HCl from the organic CDPM. With 37% Aq. HCl and CDPM densities of 1180 and 1193 kg/m^3, respectively, the decanter achieves a 30-minute residence time with a settling velocity of 0.000049 m/s. The calculated fluid volume is 358.02 L, increased by 15% to 415 L, in a horizontal cylinder with a 0.28 m radius and 1.68 m length. The output streams are 443.577 kg of aqueous waste (0.297 HCl and 0.703 water) and 220.02 kg of CDPM product.

Batch Decanter (DC-401)

DC-401 separates free-base DPH from Reactor 3 effluent. Hexane is pumped in a 4:1 ratio of hexane to Reactor 3 effluent volumetric flow ratio. The organic phase (free-base DPH, hexane, and neutral byproducts/DMAE) has a density of 750 kg/m^3, while the aqueous phase (mostly water with NaOH and NaCl) has a density of 1,110 kg/m^3. The decanter is sized for a liquid volume of 1,959.28 L, increased by 15% to 2,356.19 L, and is designed as a horizontal cylinder with a 0.49 m radius and a 3 m length (L/D ratio of 3:1). A settling velocity of 0.000577 m/s gives a residence time of 20 minutes. The decanter produces 937.96 kg of aqueous waste (87.51% water with remaining NaOH and NaCl) and 824.77 kg of organic product (33.61% freebase DPH, 64.86% hexane, plus neutral byproducts/DMAE).

Decanter Settling Velocity[20]

d_p = particle diameter (Assumed 2.5 x 10^{-9} m)
ρ_p = density of organic phase
ρ_f = density of aqueous phase
g = acceleration due to gravity
μ = viscosity of fluid

$$V = \frac{(\rho_p - \rho_f)\, g\, d_p^2}{18\, \mu} \qquad \text{Eq. DC.1}$$

Mixer (M-301)

The output from Reactor 3 is pumped into a mixer, where it is mixed with heated aqueous 3M NaOH. Reactor 3 provides 321.5 kg of product containing mass fractions of 0.015 DMAE, 0.9854 DPH·HCl ($C_{17}H_{22}ClNO$), and 0.025 neutral byproducts. In the mixer, all the components remain liquid, and the temperature is maintained at 175°C and pressure at 17.24 bar to ensure uniform mixing in the liquid phase and avoid partial crystallization of the molten salt.

The mixing process runs for 5 minutes. Given a total liquid volume of 1150 L and a 15% safety margin, the mixer is sized to 1350 L. The mixer is designed with a 2:1 height-to-diameter ratio, which results in a diameter of 0.951 m and a height of 1.90 m. For mixing, a pitch blade turbine impeller is used because it is ideal for liquid–liquid mixing under turbulent flow conditions. The impeller operates at 300 RPM because the liquids have low viscosities. The Reynolds number was calculated using Eq. M.2. The Reynolds number was found to be 592,250, which is turbulent flow. The power requirement was calculated using Eq. M.1 the formula. The power number was found using Figure 30.7 in Welty[18] for turbulent flow with a paddle impeller, which was estimated to be 2.3. The power requirement for this mixer was calculated to be 593.6 W.

Power Formula[21]

P_n: impeller power number (geometry factor)
n: impeller rotational speed
d: impeller diameter
ρ = fluid density

$$P_i = P_n \, n_3 \, p \, d_b \qquad \text{Eq. M.1}$$

Reynolds Number

N = impeller rotational speed
D = impeller diameter
ρ = fluid density
μ = dynamic viscosity (Pa s)

$$Re = \frac{N \, D^2 \, p}{\mu} \qquad \text{Eq. M.2}$$

Crystallizer

The crystallizer consists of three consecutive continuous stirred tank reactors (CSTR). The temperatures of the three tanks are based on the solubilities of similar amine salts[13]. The other major assumption for the crystallizer is that free-base DPH and DPH·HCl have equivalent heat capacities, as the presence of HCl negligibly changes this value. The residence times for the three stages are the same as those used by Snead & Jamison[4] and can be found in Table 7. Our crystallizer is primarily based on their DPH·HCl purification procedure. Therefore, we assume the same yield and purity that they obtained, which are 90% yield and over 95% purity for a single pass through the whole crystallizer unit. To achieve pharmaceutical purity of greater than 98% the product will be recycled through the crystallizer a second time after washing in filter F-401. The tanks are held at a pressure of 6 bar and made of Hastelloy C276 to accommodate the corrosive nature of HCl. The tanks are temperature controlled using jackets with steam and glycol for heating and cooling, respectively. Jacketed cooling and heating is ideal given the required surface area for heat transfer is less than the surface area of the tank. The heat duties and required utilities for each tank were simulated by HeatX blocks in Aspen Plus v14.

To determine the amount of HCl/IPA solution required, a stoichiometric balance was done with a 1:1 molar ratio of HCl to free-base DPH and a 1:1 molar ratio of HCl to free-base DPH. Each mole of free-base DPH needs 1 mole of HCl to form DPH·HCl, and each mole of free-base DMAE needs 1 mole of HCl to become DMAE·HCl. Therefore, we determined an exact molar requirement of HCl to be 1138.2 mol/h. The minimum required volume of HCl/IPA solution is 228 L/h. To ensure complete protonation, HCl/IPA solution is added in 21.6% excess for a total of 277.4 L/h of solution. Calculations for the stoichiometric balance can be found in the Appendix.

In the first tank, decanter DC-401 effluent is mixed with an HCl/IPA solution at 50°C. This step allows the reaction between free-base DPH and HCl to go to completion, and the high temperature ensures that the mixture is completely dissolved. The DPH reaction with HCl occurs nearly instantaneously, requiring a residence time in this tank of only 2 minutes. The heat duty required to heat the mixture from ambient temperature to 50°C is 29 kW, and the minimum required surface area for heat transfer is 0.3 m^2. The heating is done using 5 bar saturated steam at 48.6 kg/h, which will condense and exit the jacket as water in vapor-liquid equilibrium at 5 bar and 142°C.

In the second tank, the mixture is cooled from 50°C to 25°C, causing the mixture to become supersaturated and thereby inducing nucleation. This cooling can occur relatively quickly, requiring a residence time of 5 minutes for the mixture to become supersaturated. The heat duty required to cool the mixture from 50°C to 25°C is 29 kW, and the minimum required surface area for heat transfer is 1.0 m^2. Cooling of the tank will be done using -5°C glycol at 2905 kg/h, which will exit the jacket at 10.8°C.

In the third and final tank of the crystallizer, the mixture is further cooled from 25°C to 5°C to allow the nuclei to fully develop into the crystal form of our final product. This cooling step should occur slower than the previous step to ensure consistency and purity of the crystals. Therefore, the residence time in this tank is 16 minutes. The heat duty required to cool the mixture from 25°C to 5°C is 24 kW, and the minimum required surface area for heat transfer is 1.0 m^2. The cooling is done using -30°C glycol at 1117 kg/h, which will exit the jacket at 4.2°C.

Finally, the three tanks were sized and designed for solid suspension mixing. Marine impellers were chosen to promote axial mixing. The tank volume was calculated as the product of the flow rate and residence time with an added 15% headspace. The tanks were sized according to the following assumptions: 2:1 ratio of height to diameter, 3:1 ratio of tank diameter to impeller diameter, and 3:1 ratio of tank height to impeller height from base. Four baffles were also added to each tank to promote mixing. The baffles extend 1/10th of the tank diameter into the center of the tank, and they are 1/20th of the diameter in width[14]. The results are shown in Table 7 below, and calculations can be found in the Appendix.

Table 7. Crystallizer tank designs

	Tank 1	**Tank 2**	**Tank 3**
Residence Time (min)	2	5	16
Flow rate (L/min)	24.8	24.8	24.0
Tank Volume (L)	57.04	142.6	441.6
Tank Height (m)	0.66	0.90	1.3
Tank Diameter (m)	0.33	0.45	0.66
Impeller Height from Base (m)	0.22	0.30	0.44
Impeller Diameter (m)	0.11	0.15	0.22
Baffle Dimensions (4x) (m)	0.03 x 0.017	0.045 x 0.0225	0.066 x 0.033

Centrifugal Pumps, Blowers, Compressors, and Screw Feeders

All pumps are centrifugal pumps designed to handle the required flow rates and pressures between each unit operation. Each pump was designed with the assumption that there were no elevation differences between unit operations, resulting in the most required pressure difference primarily overcoming frictional losses and control valve loss. Each pump has an assumed pressure loss of 0.5 atm for friction in pipes, 0.5 atm for each heat exchanger (if applicable), and ⅓ of the total frictional loss for a control valve, which all centrifugal pumps require. Every pump will have an efficiency of 70% to account for the loss due to the motors. An electrical efficiency of 90% was also assumed.[22] Eq P.1 was used to calculate the total pressure differential. Eq P.2 was used to determine the pump power requirements.

Compressors were also designed to transport gases from lower pressure to higher pressure. They were modeled in Aspen Plus v14 using the Multi-Compr essor Unit Block increasing the pressure to the pressure of the condensers. Each compressor has two stages and was modeled as isentropic. After compressing the gases, the temperature was stabilized by a one stage cooling system within the Multi-Compressor Unit Block that lowers the temperature back to its original temperature. This ensures that the temperature entering the condensers is the correct temperature.

Blowers were designed using Eq. P.3, which utilizes the airflow, static pressure, a power conversion factor of 6356 to convert to hp, and an efficiency of 70% to account for the loss due to motors. 1 bar of pressure translated to a static pressure of 406.08 inch H2O. The power number was then converted to kW from hp.

All screw feeders are designed to handle the required flow rates of solids between each unit operation. Since it was calculated that the power required for the screw feeders was negligible, all screw feeders were designed to have a screw pitch of 0.5 meters and a length of 10 meters[23].

Differential Pressure Calculations

P = pressure in bar

$$\Delta P = \Delta P_{units} + P_{pipeloss} + P_{CVloss} * 100000 \frac{Pa}{bar}$$ Eq P.1

Power Equation

V = Volumetric Flow Rate
P = Differential Pressure

$$Power(W) = \frac{\dot{V}}{\Delta P}$$ Eq P.2

Blower Equation[30]

η = efficiency - assume 70%
Air flow = ft^3/min
Static pressure = in water column

$$FanPower(hp) = \frac{AirFlow * StaticPressure}{6356 * \eta}$$ Eq P.3

Table 8. Pumps Block 1

Equipment name	Feed (kg)	Power (kW)	Pressure In (bar)	Pressure Out (bar)
P-101	356.9	0.02	1	1
P-102	205.1	0.01	1	1
P-103	800.0	0.04	1	1
P-104	2507.9	0.11	1	1
CP-101	2789.8	354.59	1	15
B-101	2938.7	96.33	1	1

Table 9. Pumps Block 2

Equipment name	Feed (kg)	Power (kW)	Pressure In (bar)	Pressure Out (bar)
P-201	463.6	0.40	1	15
P-202	220.0	0.01	1	1

Table 10. Pumps Block 3

Equipment name	Feed (kg)	Power (kW)	Pressure In (bar)	Pressure Out (bar)
P-301	220.02	0.10	1	17.2
P-302	101.46	0.12	1	17.2
P-303	321.50	0.01	17.2	17.2
P-304	898.30	0.54	1	17.2

Table 11. Pumps Block 4

Equipment name	Feed (kg)	Power (kW)	Pressure In (bar)	Pressure Out (bar)
P-401	1227.79	0.05	1	1
P-402	534.94	0.04	1	1
P-403	824.77	0.28	1	6
P-404	269.04	0.09	1	6
P-405	264.24	0.02	1	1
P-406	1248.10	0.08	1	1
P-408	124.70	0.36	1	6
CP-401	2122.40	307.82	1	20

Storage Tanks

All storage tanks were designed to have enough storage capacity for 5 batches, with the exception of storage tanks for product intermediates, which are designed to hold one batch. This batch capacity was chosen because the plant will run continuously 24 hours a day and can complete roughly 5 batches in 24 hours. Thus, the tanks can be refilled once a day and supply reactants for the entire production day. Tank volume was determined based on the liquid volume with an additional 15% for safety. Tank diameter and height were determined with a 2:1 ratio. Nitrogen tanks are split into 4 separate tanks. Pressure was determined with ideal gas law as seen in equation T.1. Due to the nitrogen recycle storage tanks are designed to hold ⅓ of full nitrogen requirements for a single batch.

Ideal Gas Equation for Nitrogen Tank Pressure

P = Pressure
V = Volume
n = moles
R = gas constant
T = Temperature

$$PV = nRT \qquad \text{Eq T.1}$$

Tank Radius Dimensions for 2:1 diameter:height

V = Volume
R = Tank Radius

$$R = \left(\frac{V}{4\pi}\right)^{\frac{1}{3}} \qquad \text{Eq T.2}$$

Table 12-a. Tank Designs in Block 1

Tank	**T-101 (meth)**	**T-102 (Benzo)**	**T-103 (NaBH4)**	**T-104 (DM H2O)**	**T-105 (waste)**	**T-107 (benzhyd)**
Liquid volume (L)	2257	1024.5	782	12000	14290	220.6
Tank Volume (L)	2596	1178	899.3	13800	16433.5	253.69
Tank Volume (m^3)	2.6	1.18	0.9	13.8	16.43	0.25
Tank r (m)	0.591	0.454	0.415	1.032	1.094	0.272
Tank d (m)	1.182	0.91	0.830	2.063	2.187	0.545
Tank h (m)	2.364	1.817	1.661	4.127	4.374	1.089
MOC	A316 stainless steel	A316 stainless steel	A316 stainless steel	A316 stainless steel	A316 stainless steel	A316 stainless steel

Table 12-b. Nitrogen Tanks Design in Block 1

Tank	**T-106 (a-d) (N2) (P=14.75 bar) (T = 298.15 K)**
N2 per batch (kg)	2400.45
⅓ of N2 used (kg)	800.15
Tank pressure (bar)	14.75
Volume of each tank (m^3)	12
Number of tanks	4
Tank r (m)	0.98
Tank d (m)	1.97
Tank h (m)	3.94
MOC	A316 stainless steel

Table 13. Tank Designs in Block 2

Tank	**T-201 (aq HCl)**	**T-202 (chloro.)**
Liquid volume (L)	2916.75	193
Tank Volume (L)	3354.2	222
Tank Volume (m^3)	3.35	0.22
Tank r	0.64	0.26
Tank d	1.29	0.52
Tank h	2.58	1.042
MOC	Hastelloy	A316 stainless steel

Table 14. Tank Designs in Block 3

Tank	**T-301 (DMAE)**	**T-302 (Aq NaOH)**	**T-303 (crude DPH)**
Liquid volume (L)	717.4	4046.41	1150
Tank Volume (L)	825.01	4653.3715	1322.5
Tank Volume (m^3)	0.825	4.653	1.323
Tank r	0.403	0.718	0.472
Tank d	0.807	1.436	0.944
Tank h	1.614	2.872	1.889
MOC	A316 stainless steel	A316 stainless steel	A316 stainless steel

Table 15-a. Tank Designs in Block 4

Tank	T-401 (hexane)	T-402 (HCl/IPA)	T-403 (waste)	T-404 (waste II)	T-406 (Pure DPH)
Liquid volume (L)	8046.4	1386.8	4270	8975	255.45
Tank Volume (L)	9253.36	1594.82	4910.5	10321.25	293.76
Tank Volume (m^3)	9.25	1.59	4.91	10.32	0.29
Tank r	0.90	0.50	0.73	0.94	0.29
tank D	1.81	1.01	1.46	1.87	0.57
Tank h	3.61	2.01	2.92	3.75	1.14
MOC	A316 stainless steel	Hastelloy	A316 stainless steel	A316 stainless steel	A316 stainless steel

Table 15-b. Nitrogen Tanks Design in Block 4

Tank	T-405 (a-d) (N2) (P=14.75 bar) (T = 298.15 K)
N2 per batch (kg)	2000
⅓ of N2 used (kg)	666.67
Tank pressure (bar)	14.75
Volume of each tank (m^3)	10
Number of tanks	4
Tank r (m)	0.93
Tank d (m)	1.85
Tank h (m)	3.71
MOC	A316 stainless steel

6. Plant Schedule Discussion

The plant will operate 24 hours per day for 313 days each year. Every six weeks, the plant will shut down for a one-week cleaning period. The cleaning schedule begins on January 22nd each year. There will be eight cleaning shutdowns and eight post-cleaning start-ups annually. The cleaning weeks are scheduled for January 22-28, March 5-11, April 16-22, May 28-June 3, July 9-15, August 20-26, October 1-7, and November 12-18, as well as December 24-30.

This specific January 22nd start date was chosen because it allows Christmas to fall during a cleaning week, which reduces the number of additional shutdown and start-up days needed. This six-week cycle will repeat in the same pattern each year. During leap years, one interval in the year will be 41 days instead of the usual 42 days to maintain the schedule.

In addition to the eight cleaning periods, the plant will also shut down for two holidays: New Year's Day and Thanksgiving. This brings the total number of plant shutdowns to ten per year.

Additionally, the starting material and reactant storage tanks will be refilled after every five batches, which is approximately once per day.

7. Waste Management and Environmental Concerns

Waste Treatment

Block 1 produces three main waste streams. First, 7.16 kg/h of hydrogen gas is captured and purified using a pressure swing adsorption (PSA) system to achieve greater than 99.9% purity. Second, the "dirty water" stream flows at 2617 kg/h and is 92.6% water, 0.4% benzophenone, 0.79% methanol, and 7.1% sodium tetra-methyl borate ($NaB(OCH_3)_4$). This mixture is transferred to a neutralization tank, where a 5–10% HCl solution from Block 2 is added to neutralize the waste water and adjust the pH to roughly 6–8. The solids are then filtered out. The slurry is sent to a certified waste management company. Finally, 1016 kg/h of DM water vapor is vented, with proper monitoring to ensure compliance with environmental regulations.

Block 2 produces 444 kg/h of an acid-water mixture from the decanter, which is 29.7% HCl and 70.3% water. Some of the acid mixture is sent to Block 1 waste treatment to neutralize the alkaline wastewater, and another portion is directed to Block 4 to neutralize the sodium hydroxide waste. The decanter also separates out minor organic residues, such as unreacted Benzhydrol, which are collected for disposal by a certified waste management company. By reserving this acid-water stream for targeted neutralization in other blocks, we minimize the introduction of additional chemicals, while ensuring each waste stream is treated effectively.

In Block 4, two waste streams are generated. The first is 938 kg/h of the decanter aqueous waste, which is 87.51% water, 5.27% NaOH, and 6.77% NaCl. The NaOH is neutralized with 49 kg/h of HCl from Block 2 to form NaCl before being sent to a certified waste management company. The second stream is 1367 kg/h of filter waste, which is 77.38% hexane, 16.64% IPA, 3.03% HCl, 2% free‑base DPH, 0.58% neutral byproducts, and 0.34% DMAE. The composition of the neutral byproducts are Diphenylmethane, 1,1′,2,2′‑Tetraphenylethane, Benzophenone[4]. This stream is collected as‑is and shipped off‑site for disposal due to its combination of solvents, acids, and residual amines. By following these procedures, Block 4 ensures compliance with environmental regulations while maintaining safe handling of both aqueous and organic waste streams.

8. Health and Safety

Quality Control

Our plant will conform to the FDA’s Code of Federal Regulations (CFR) including their current Good Manufacturing Practice in Manufacturing Processing, packing, or Holding of Drugs described in Title 21 CFR Part 210[24], as well as Current Good Manufacturing Practice for Finished Pharmaceuticals described in Title 21 CFR part 211[25].

Our product purity will be tested for each batch using ^{1}H NMR spectroscopy using tetramethylsilane (TMS) as an external standard.

Hazard Information

In Block 1, the primary hazards pertain to solids handling and flammability. Benzophenone is also carcinogenic. Sodium borohydride is a toxic and flammable solid. Methanol and hydrogen are both very flammable, and methanol is also toxic. Detailed chemical hazard information for Block 1 can be found in Table 16. In Block 2, the primary hazards are the toxicity of hydrogen chloride and chlorodiphenylmethane. Hydrogen chloride is also highly corrosive to metals, so corrosion-resistant nickel alloys will be used for equipment in contact with hydrogen chloride. Detailed chemical hazard information for Block 2 can be found in Table 17. In Block 3, dimethylaminoethanol is toxic and flammable, and sodium hydroxide is toxic and corrosive to some metals. Detailed chemical hazard information for Block 2 can be found in Table 18. In Block 4, both hexane and isopropanol are toxic, flammable solvents. Detailed chemical hazard information for Block 4 can be found in Table 19.

Table 16. Block 1 Chemical SDS Information

Table 16.	**BLOCK 1**				
Chemical Name	**Benzophenone**	**Sodium Borohydride**	**Methanol**	**Hydrogen**	**Sodium Tetramethoxyborate**
CAS	119-61-9	16940-66-2	67-56-1	1333-74-0	18024-69-6
Formula	$C_{13}H_{10}O$	H_4BNa	CH_4O	H_2	$C_4H_{12}BO_4 \cdot Na$
Signal Word	Danger	Danger	Danger	Danger	Warning
Hazard Statements	H350 May cause cancer	H260 In contact with water releases flammable gases which may ignite spontaneously	H225 Highly flammable liquid and vapor	H220 Extremely flammable gas	H315 Causes skin irritation
	H373 May cause damage to organs (Liver, Kidney) through prolonged or repeated exposure if swallowed	H301 Toxic if swallowed	H301 H311 H331 Toxic if swallowed, in contact with skin or if inhaled	H280 Contains gas under pressure; may explode if heated	H319 Causes serious eye irritation
	H412 Harmful to aquatic life with long lasting effects	H314 Causes severe skin burns and eye damage	H370 Causes damage to organs (Eyes, Central nervous system)	May displace oxygen and cause rapid suffocation	H335 May cause respiratory irritation
		H360 May damage fertility or the unborn child		Burns with invisible flame	
		H402 Harmful to aquatic life		May form explosive mixtures with air	

Table 16.	**BLOCK 1**				
Chemical Name	**Benzophenone**	**Sodium Borohydride**	**Methanol**	**Hydrogen**	**Sodium Tetramethoxyborate**
Pictograms					
NFPA					
Exposure Limits			TLV-TWA 200 ppm STEL 250 ppm C 1000 ppm		
Flammability Limits		LEL: 3.02 V%	UEL: 44 V% LEL: 5.5 V%	UEL: 77 V% LEL: 4 V%	
Threshold Release Category (TRC)		TRC-8 (H314)	TRC-3 (H331)	TRC-5 (H220)	
API-754 TQs (Tier 1, indoor)			10 kg	50 kg	
Codes & Regulations	Annex XVII of REACH	SARA 311 and 312	CERCLA RQ, SARA 311 312 313	SARA 311 and 312	
SDS Hyperlinks	Sigma Aldrich	Sigma Aldrich	Sigma Aldrich	Sigma Aldrich	Biosynth
	Gustavus Education			Harper College	

Table 17. Block 2 Chemical SDS Information

Table 17.	BLOCK 2	
Chemical Name	**Hydrogen Chloride**	**Chlorodiphenylmethane**
CAS	7647-01-0	90-99-3
Formula	HCl	C13H11Cl
Signal Word	Danger	Danger
Hazard Statements	H290 May be corrosive to metals	H314 Causes severe skin burns and eye damage
	H314 Causes severe skin burns and eye damage	
	H335 May cause respiratory irritation	
Pictograms		
NFPA		
Exposure Limits	TLV-C 2 ppm PEL-TWA 0.3 ppm IDLH 50 ppm	N/A
Flammability Limits	N/A	N/A
TRC	TRC-8 (H314)	TRC-8 (H314)
API-754 TQs (Tier 1, indoor)	N/A	N/A
PSM TQs	5000 lbs	Not covered
Codes & Regulations	SARA 311 312 313	
SDS Hyperlinks	Sigma Aldrich	Fisher Sci
		Sigma Aldrich

Table 18. Block 3 Chemical SDS Information

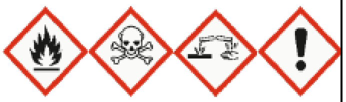
Table 18.	BLOCK 3			
Chemical Name	**Dimethylaminoethanol**	**NaOH**	**DPH HCL**	**DPH**
CAS	108-01-0	1310-73-2	147-24-0	58-73-1
Formula	$C4H11NO$	$NaOH$	$C17H21NO \cdot HCl$	$C17H21NO$
Signal Word	Danger	Danger	Warning	Warning
Hazard Statements	H226 Flammable liquid and vapor	H290 May be corrosive to metals	H302 Harmful if swallowed	H302 Harmful if swallowed
	H302 H312 Harmful if swallowed or in contact with skin	H314 Causes severe skin burns and eye damage		
	H314 Causes severe skin burns and eye damage	H402 Harmful to aquatic life		
	H331 Toxic if inhaled			
	H335 May cause respiratory irritation			
	H402 Harmful to aquatic life			
Pictograms				
NFPA				
Exposure Limits		TLV-C 1.22 ppm IDLH 6.11 ppm		Pfizer TWA 0.015 ppm
Flammability Limits	LEL: 1.4 V% UEL: 12.2 V%			
TRC	TRC-3 (H331)	TRC-8 (H314)		
API-754 TQs	10 kg			
Codes & Regulations	SARA 311 and 312	CERCLA RQ Clean Water Act Section 311	SARA 311 and 312	
SDS Hyperlinks	Sigma Aldrich	Sigma Aldrich	Sigma Aldrich	Tci Chemicals
	Fisher Sci	Fisher Sci	Fisher Sci	Pfizer

Table 19. Block 4 Chemical SDS Information

Table 19.	**BLOCK 4**	
Chemical Name	**Hexane**	**Isopropanol**
CAS	110-54-3	67-63-0
Formula	C6H14	C3H8O
Signal Word	Danger	Danger
Hazard Statements	H225 Highly flammable liquid and vapor	H225 Highly flammable liquid and vapor
	H304 May be fatal if swallowed and enters airways	H319 Causes serious eye irritation
	H315 Causes skin irritation	H336 May cause drowsiness or dizziness
	H336 May cause drowsiness or dizziness	
	H361 Suspected of damaging fertility or the unborn child	
	H373 May cause damage to organs (Nervous system) through prolonged or repeated exposure if inhaled	
	H411 Toxic to aquatic life with long lasting effects	
Pictograms		
NFPA		
Exposure Limits	TLV-TWA 50 ppm IDLH 1100 ppm	TLV-TWA 200 ppm IDLH 2000 ppm
Flammability Limits	LEL: 1.1 V% UEL: 7.5 V%	LEL: 2 V% UEL: 12.7 V%
Threshold Release Category	TRC-6 (H225)	TRC-6 (H225)
API-754 TQs (Tier 1, indoor)	100 kg	100 kg
Codes & Regulations	CERCLA RQ, SARA 313	Clean Air Act: 40 CFR 61
SDS Hyperlinks	Airgas Sigma Aldrich	Sigma Aldrich

Reactivity Information

The reactivity matrix completed using Cameo Chemicals, which is depicted in Figure 11, shows that there are many hazardous reactions that could occur. While many of the identified incompatible chemicals are not intended to be mixed, they will still be stored, transported, and processed within the same facility. Therefore, it is essential to implement safeguards to prevent and mitigate any unintended chemical interactions. A * indicates that the reactive mixture is an intended reaction in our process that will take place in controlled conditions.

Key incompatibilities include the following:

Benzophenone when mixed with methanol*, 2-dimethylaminoethanol, or isopropanol can become explosive and unstable when heated.

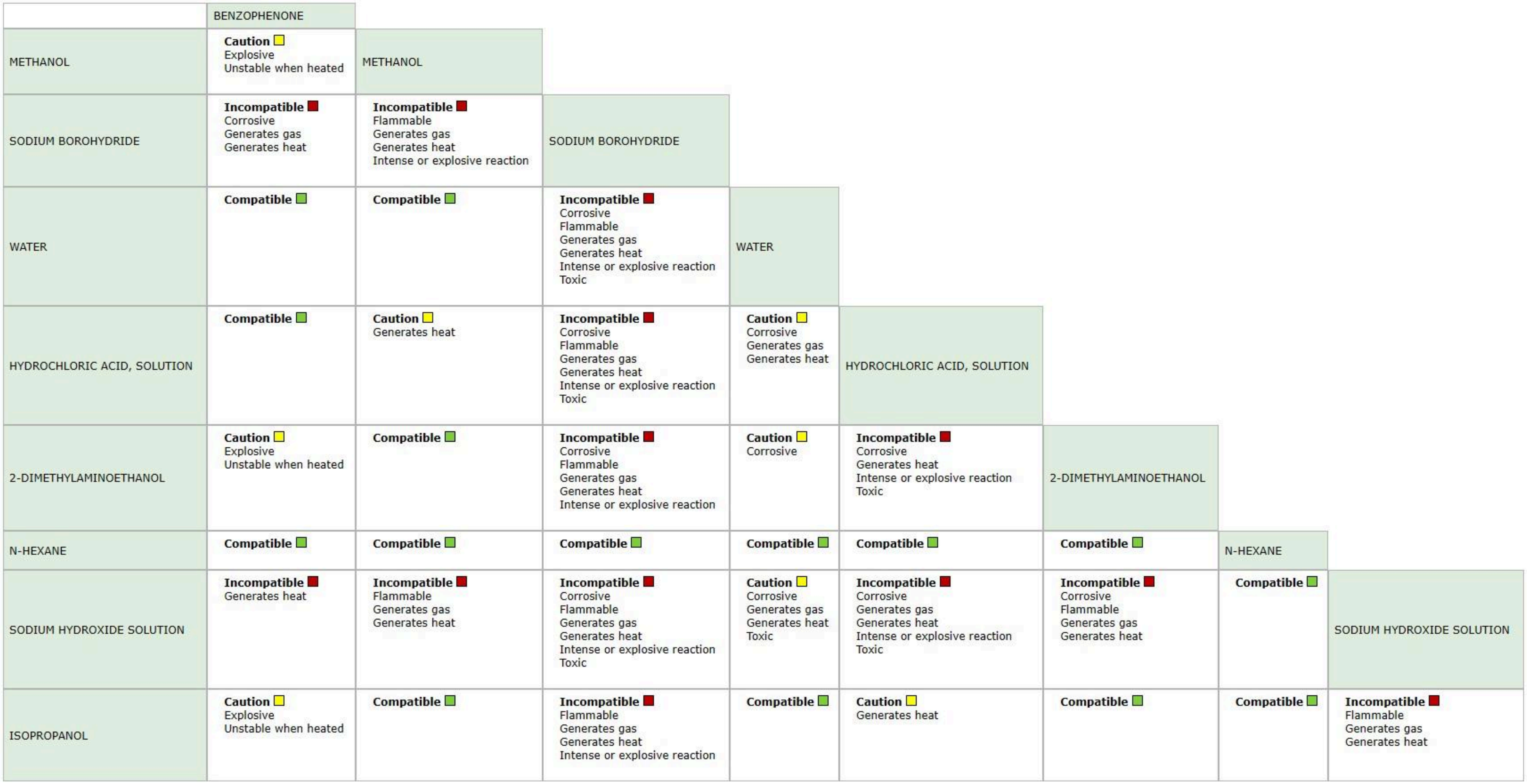
Sodium borohydride when mixed with methanol* generates gas and heat, leading to a corrosive, flammable, and potentially explosive reaction with toxic byproducts.

Sodium borohydride when mixed with water causes a corrosive, flammable reaction that generates heat and toxic gas, potentially becoming explosive.

Sodium hydroxide solution when mixed with benzophenone or methanol generates significant heat, creating hazardous conditions.

Sodium hydroxide solution when mixed with sodium borohydride, hydrochloric acid solution, 2-dimethylaminoethanol*, or isopropanol results in corrosive, flammable reactions with gas and heat generation, potentially becoming explosive and producing toxic byproducts.

Isopropanol when mixed with sodium borohydride generates gas and heat, resulting in a flammable and potentially explosive reaction.



	BENZOPHENONE							
METHANOL	**Caution** 🟨 Explosive Unstable when heated	METHANOL						
SODIUM BOROHYDRIDE	**Incompatible** 🟥 Corrosive Generates gas Generates heat	**Incompatible** 🟥 Flammable Generates gas Generates heat Intense or explosive reaction	SODIUM BOROHYDRIDE					
WATER	**Compatible** 🟩	**Compatible** 🟩	**Incompatible** 🟥 Corrosive Flammable Generates gas Generates heat Intense or explosive reaction Toxic	WATER				
HYDROCHLORIC ACID, SOLUTION	**Compatible** 🟩	**Caution** 🟨 Generates heat	**Incompatible** 🟥 Corrosive Flammable Generates gas Generates heat Intense or explosive reaction Toxic	**Caution** 🟨 Corrosive Generates gas Generates heat	HYDROCHLORIC ACID, SOLUTION			
2-DIMETHYLAMINOETHANOL	**Caution** 🟨 Explosive Unstable when heated	**Compatible** 🟩	**Incompatible** 🟥 Corrosive Flammable Generates gas Generates heat Intense or explosive reaction	**Caution** 🟨 Corrosive	**Incompatible** 🟥 Corrosive Generates heat Intense or explosive reaction Toxic	2-DIMETHYLAMINOETHANOL		
N-HEXANE	**Compatible** 🟩	**Compatible** 🟩	**Compatible** 🟩	**Compatible** 🟩	**Compatible** 🟩	**Compatible** 🟩	N-HEXANE	
SODIUM HYDROXIDE SOLUTION	**Incompatible** 🟥 Generates heat	**Incompatible** 🟥 Flammable Generates gas Generates heat	**Incompatible** 🟥 Corrosive Flammable Generates gas Generates heat Intense or explosive reaction Toxic	**Caution** 🟨 Corrosive Generates gas Generates heat Toxic	**Incompatible** 🟥 Corrosive Generates gas Generates heat Intense or explosive reaction Toxic	**Incompatible** 🟥 Corrosive Flammable Generates gas Generates heat	**Compatible** 🟩	SODIUM HYDROXIDE SOLUTION
ISOPROPANOL	**Caution** 🟨 Explosive Unstable when heated	**Compatible** 🟩	**Incompatible** 🟥 Flammable Generates gas Generates heat Intense or explosive reaction	**Compatible** 🟩	**Caution** 🟨 Generates heat	**Compatible** 🟩	**Compatible** 🟩	**Incompatible** 🟥 Flammable Generates gas Generates heat

Figure 11. Reactivity Matrix using Cameo Chemicals

Credible Safety Events

To determine the potential consequence of three major credible release scenarios, we used the computer modeling software Areal Locations of Hazardous Atmospheres (ALOHA). ALOHA models the dispersion of toxic gasses, the effects of thermal radiation, and explosions. It can also be used in conjunction with MARPLOT to find the threat zones for gas releases. It is part of the software developed by the Environmental Protection Agency (EPA) and National Oceanic and Atmospheric Association (NOAA). For this project, we are using ALOHA to model credible process safety events that could occur during our process and to determine the MCE.

Table 20. Average Weather Characteristic throughout the 2024 Year[26]

Month	Temperature (F) Day/night	Wind Speed (mph)/direction	Cloud coverage (%)	Humidity (%)	Day stability class	Night stability class
January	41/26	10.5 S	42	0	C	D
February	44/28	11.0 S	45	0	C	D
March	55/36	12.1 S	43	0	C	D
April	67/45	12.3 S	37	5	C	D
May	75/53	11.1 S	38	18	C	D
June	82/62	10.4 S	33	55	C	D
July	85/65	9.6 S	27	70	C	D
August	84/64	9.1 S	28	65	C	D
September	77/57	10.2 S	29	18	C	D
October	66/46	10.8 S	31	5	C	D
November	55/37	10.9 S	38	0	C	D
December	45/30	10.4 S	42	0	C	D

Table 20 depicts the conditions for the 2024 seasonal year at Ponca City, Oklahoma. Each credible scenario was modeled at 3:00 AM on November 1, 2024 because this is a conservative estimate that maintains a night stability class of an E (highlighted in yellow in Table 20). The ground coverage in this location is urban and forest, with a wind speed of 3 mph coming from the East-Southeast direction. The specific time was determined because it favors a stable atmosphere with low turbulent wind flow.

Event 1: Hydrogen Gas Unloading and Loading Hose Failure

Hydrogen gas is produced in Reactor 1 from a side reaction between methanol and sodium borohydride. The hydrogen must be properly managed and transferred to proper treatment facilities. During this process, accidents can occur, resulting in hydrogen being leaked due to a full bore rupture of the hose or hose connection. Due to hydrogen's extreme flammability, ignition sources could include heat, electric equipment, and reactions with strong oxidizers. Thus, a release would cause a high-risk fire hazard. Based on Figure 12, the ALOHA model predicts that the hydrogen could travel up to 213 yards and has a high probability of igniting at up to 92 yards.

Event 2: Liquid Methanol Unloading and Loading Hose Failure

Methanol is used as a solvent in Reactor 1. During the refilling and transportation of materials, accidents can occur, resulting in methanol being leaked due to a full bore rupture of the hose or hose connection. Due to methanol's high flammability, ignition sources could include heat, electric equipment, and reactions with strong oxidizers. Thus, a release would pose a significant fire hazard. Based on Figures 13 and 14, the ALOHA model predicts that the methanol vapor could travel up to 1142 yards, with high concentrations of 5000 ppm up to 286 yards. Methanol gas can also travel up to 242 yards before catching fire and has a high probability of igniting at up to 82 yards.

Event 3: Liquid Hexane Unloading and Loading Hose Failure

Hexane is used in the decanter and second wash and filter step to separate the inorganic and organic layers. Since hexane is being used and transferred throughout Block 4, accidents can occur, resulting in hexane being leaked due to a full bore rupture of the hose or hose connection. Due to hexane being flammable, ignition sources could include heat, electric equipment, and reactions with strong oxidizers, which poses a fire hazard. Based on Figure 15, the ALOHA model predicts that hexane could travel up to 250 yards, with high concentrations of 7200 ppm at up to 124 yards.

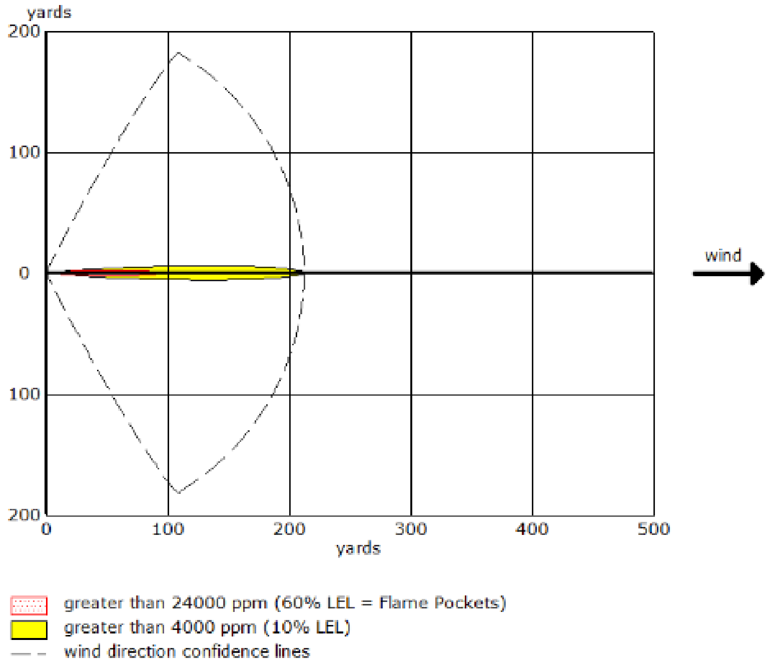


Figure 12. Aloha Simulation of a Flammable Event of Hydrogen

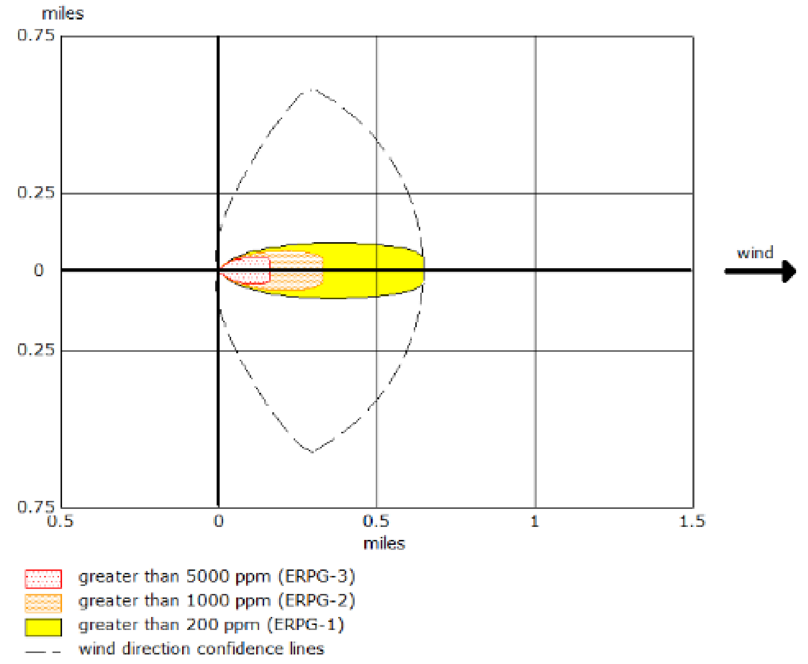


Figure 13. Aloha Simulation of Toxic Gas for Methanol Vapor

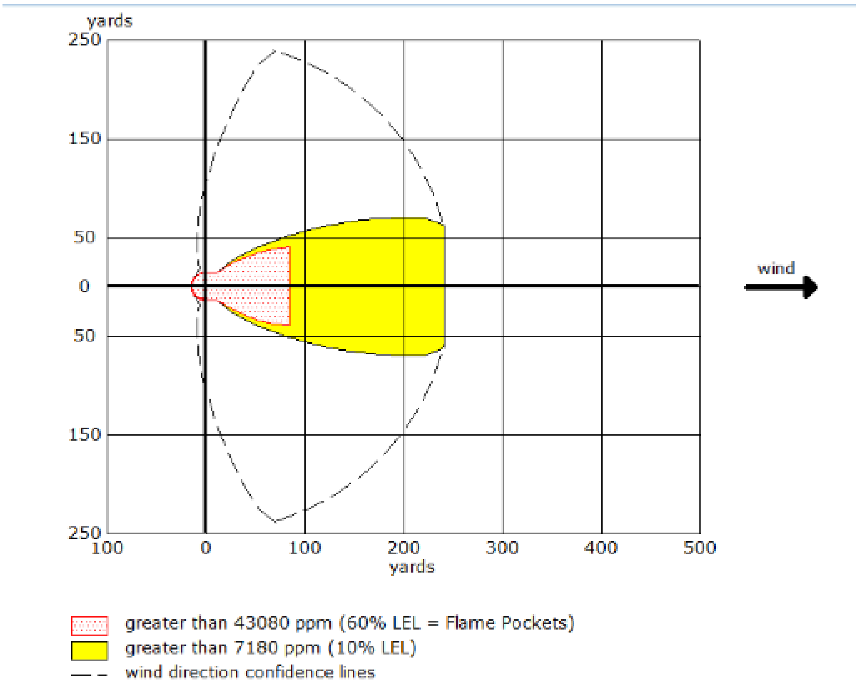


Figure 14. Aloha Simulation of a Flammable Event of Methanol

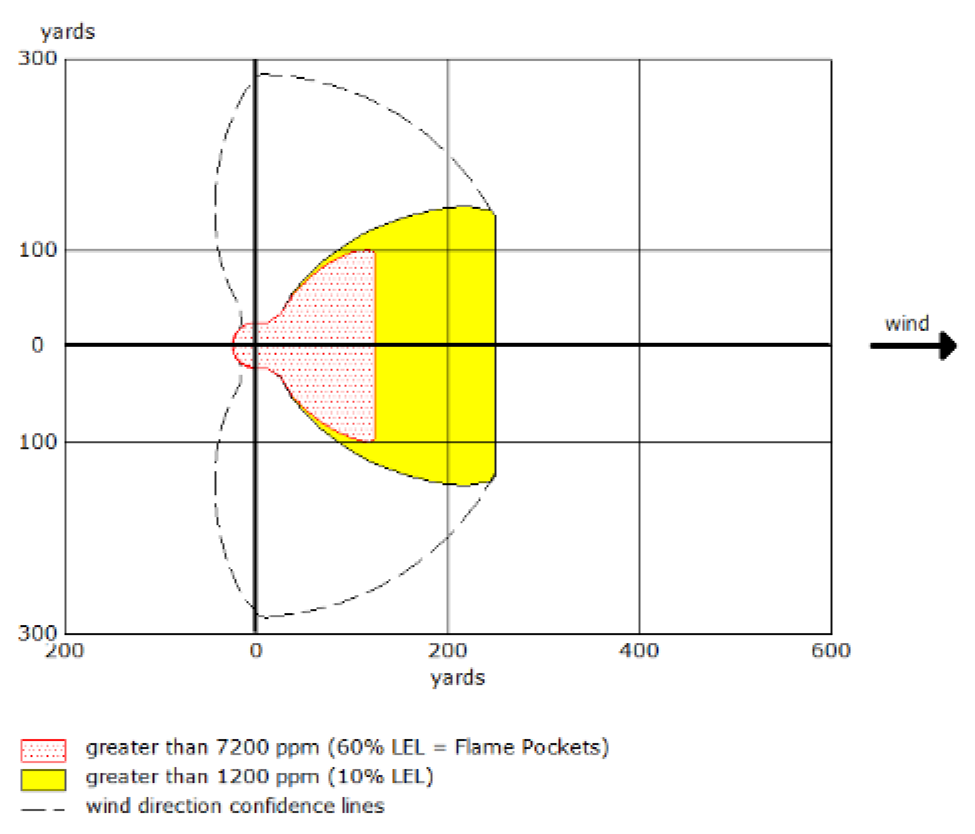


Figure 15. Aloha Simulation of a Flammable Event of Hexane

Based on the models from these three credible release scenarios, the maximum credible event (MCE) is a leak of methanol from a pipe, forming a toxic, flammable gas stream. This is the MCE because it produced the longest threat zone of all the events modeled in ALOHA. Additionally, methanol has a short flammable scope, measuring 84 yards, while this can sound like a good thing, the short travel of the vapor is due to its high likelihood of encountering an ignition source and igniting, reflecting methanol's highly volatile behaviour. Under worst-case scenario stability conditions, the toxic gas threat zone would extend up to 1,142 yards. We recommend that the storage tank be placed in a separate area, with pipes of appropriate thickness and material. Additionally, regular inspections of the pipes, connection points, and storage tanks should be conducted.

Administrative Controls

The severity of the credible release scenarios above demonstrate that proper training, procedures, and design are necessary to prevent loss of primary containment events. To minimize these and other risks, all personnel must adhere to established procedures, wear appropriate personal protective equipment (PPE), and stay informed through labels, training, and documentation.

Use of PPE such as gloves, goggles, face shields, and respirators will be strictly enforced. PPE required by Good Manufacturing Practices (GMP) will also be used. Safety Data Sheets (SDS) must be readily accessible and reviewed regularly. All workers will complete routine training refreshers that cover reading SDS documents, labeling systems, safe handling procedures, emergency response procedures, etc. Employees should know how to use PPE correctly and be knowledgeable about the equipment they work with. Regular inspections of piping, seals, and valves, especially for corrosive or flammable substances, will be conducted to reduce the risk of leaks and accidental discharges. The following PPE guidelines will be used for the specific hazards associated with hydrogen gas, methanol, and hexane.

Hydrogen is a flammable gas that can cause rapid suffocation. When working with or near this gas, it is recommended to use standard eye protection and flame-retardant, antistatic protective clothing to minimize potential ignition sources. Additionally, antistatic, non-slip safety shoes are also recommended to prevent any static buildup. Workers will also be required to wear hydrogen gas detectors near this unit.

Methanol is a flammable liquid and vapor, and it can cause damage to organs if ingested. When working with methanol, workers should wear standard eye and face protection, as well as flame-retardant, antistatic protective clothing to minimize ignition risks. Additionally, chemical-resistant gloves should be worn to prevent any skin contact or absorption. Respirators with filters should be worn if ventilation is inadequate.

Hexane is a flammable liquid and vapor and can cause rapid suffocation if inhaled. Workers should use standard eye and face protection and wear flame-retardant, anti-static clothing to prevent ignition and reduce inhalation risks. Nitrile gloves should be worn to to prevent any skin contact or absorption. Respirators with filters should be worn if ventilation is inadequate.

All chemicals must be labeled clearly in compliance with GHS standards. Employees must follow established handling and disposal procedures and be trained to recognize chemical labels and hazard pictograms. Proper signage should be placed in areas containing flammable or hazardous materials to warn against ignition sources.

Engineering Controls

Table 21: Hierarchy of Hazard Controls

Inherent Safety
Segregation and Separation
Passive Safeguards
Active Safeguards
Administrative Controls
Personal Protective Equipment
Emergency Response

In addition to all the proper procedures and inherently safer design, other safeguards must be in place to prevent incidents. Implementation of elements from throughout the hierarchy of hazard controls is required to eliminate or minimize the risk of hazardous chemicals and operations. Although inherently safer design is the most effective, some risks will not be possible to design out of the process. Thus, other safety measures, like active and passive safeguards, must be in place to minimize risk.

Passive safeguards are equipment that automatically works without requiring any action. For passive controls, our plant will implement dikes around storage vessels to contain spills and blast walls around Reactor 2 to protect against overpressure. Active controls require a human or system action to work and are therefore less reliable. For active controls, our plant will use high and low liquid level alarms, among other process control systems for each of the unit operations. Sprinklers and water deluge systems will also be installed in case of fire.

V. Final Design

1. Final Plant design and Stream Tables

Block 1

In Block 1, benzophenone is reduced into benzhydrol. Methanol, benzophenone, and sodium borohydride are fed into Reactor 1 in the quantities listed in Table 22. Methanol, a liquid, is fed via a pump. Benzophenone and sodium borohydride are solids and are fed via screw feeders. The reaction runs for two hours at 1 bar and 27°C. Hydrogen offgassing is vented and purified via pressure swing adsorption. The reactor contents are then screw fed into a dryer, where methanol is evaporated with hot nitrogen at 100°C. The vapor stream is then compressed to 15 bar and cooled to 27°C, which condenses the methanol from the nitrogen. The vapor-liquid mixture is then flashed, and each component is recycled back to its respective storage tank. The product stream, which is mostly solid out of the dryer, contains unreacted benzophenone, residual methanol, sodium tetramethoxyborate (a side product), and benzhydrol, is screw fed into a filter. In the filter, the product is washed with preheated DM water to remove the sodium tetramethoxyborate, methanol, and benzophenone. The dirty water stream goes into waste treatment to be neutralized and disposed of. The remaining wet benzhydrol is screw fed into a dryer, and the residual water is evaporated with hot air at 120°C and vented to the atmosphere. The dry product is screw fed into an intermediate storage tank. Block 1 takes 4 hours and 4 minutes to complete.

Table 22. Simplified Block 1 Product Stream Table*

Name	Methanol Feed	C13H10O feed	NaBH4 feed	R1 output	Dryer 1 output	Filter output	Dryer 2 output
Mass flow (kg)	356.9	225	44.8	619.5	435.2	327.3	200
Temperature (C)	27	27	27	27	68	50	83
Phase(s) of stream	l	s	s	70 (s) :30 (l)	s	(67) s:l (33)	s
Mass Compositions (kg)							
Benzophenone ($C_{13}H_{10}O$)	—	225	—	9.2	9.2	—	—
Sodium Borohydride ($NaBH_4$)	—	—	44.8	—	—	—	—
Methanol	356.9	—	—	205.1	20.7	—	—
Hydrogen gas	—	—	—	—	—	—	—
DM water	—	—	—	—	—	109.1	—
Benzhydrol	—	—	—	218.2	218.2	218.2	218.2
NaB(OCH3)4	—	—	—	187	187	—	—

*Full stream tables including waste streams can be found in the Appendix

Block 2

In Block 2, benzhydrol is chlorinated into CDPM. The dry benzhydrol product from Block 1 is screw fed into Reactor 2, and preheated aqueous HCl at 83°C is pumped into the reactor in quantities listed in Table 23. The reactor is then heated to 83°C and pressurized to 15 bar. The reaction is allowed to proceed under these conditions for two hours, after which a control valve is opened and the reactor pressure moves the reactor contents into a decanter. After 30 minutes in the decanter, the reactor products will separate into two liquid phases. The heavy organic layer, which is pure CDPM, is drained into an intermediate storage tank. The light aqueous layer, which contains HCl and water, is pumped into waste treatment to be neutralized. Block 2 takes 2 hours and 30 minutes to complete.

Table 23. Simplified Block 2 Product Stream Table*

Name	**37% Aq. HCl feed**	**Benhydrol feed**	**R2 output**	**Chloro product**
Mass (kg)	463.6	200	663.6	220
Temperature (C)	83	83	83	25
Phase(s) of stream	aq (l)	s	l (org) :l (aq)	l (org)
Mass Compositions (kg)				
Benzhydrol ($C_{13}H_{12}O$)	—	200	—	—
Aq. HCl	171.5	—	132	—
CDPM ($C_{13}H_{11}Cl$)	—	—	220	220
Water	292.1	—	311.6	—

*Full stream tables including waste streams can be found in the Appendix

Block 3

In Block 3, CDPM undergoes a nucleophilic substitution reaction to become DPH·HCl. The CDPM product from Block 2 and DMAE are pumped into Reactor 3 in the quantities listed in Table 24. The reaction runs for 1 hour and 12 minutes at 17.2 bar and 175°C, producing crude DPH·HCl as a molten salt. The reactor contents are then pumped into a mixer with preheated 3M aqueous NaOH at reaction temperature and pressure. The NaOH neutralizes the DPH·HCl and DMAE·HCl, and the result is a two-phase liquid mixture of water, neutral byproducts, NaCl, free-base DPH, and free-base DMAE. The neutral byproducts include are Diphenylmethane, 1,1′,2,2′-Tetraphenylethane, Benzophenone[4]. After the mixer runs for 5 minutes, a control valve is opened and the vessel pressure moves the mixture through a cooler and into a tank to be stored at room temperature before purification. Block 3 takes 1 hour and 17 minutes to complete.

Table 24. Block 3 Product Stream Table

Name	**DMAE feed**	**CDPM feed**	**R3 Output**	**Aq. 3M NaOH feed**	**Mixer output**
Mass (kg)	101.5	220	321.5	898.3	1227.8
Temperature (C)	175	175	175	175	175
Phase(s) of stream	l	l	l	1	l (org) :l (aq)
Mass Compositions (kg)					
CDPM ($C_{13}H_{11}Cl$)	—	220	—	—	—
DMAE	101.5	—	4.7	—	4.7
NaOH	—	—	—	97	53.7
DPH·HCl	—	—	308.9	—	—
Free-base DPH	—	—	—	—	277.2
Neutral Byproducts	—	—	7.9	—	7.9
H2O	—	—	—	801.5	820.8
NaCl	—	—	—	—	63.5

<u>Block 4</u>

In Block 4, the crude DPH is purified to pharmaceutical quality. The unpurified DPH mixture from Block 3 is pumped into a decanter with hexane in the quantities listed in Table 25. After 20 minutes in the decanter, the heavy aqueous layer, which contains water, NaOH, and NaCl, is drained into waste. The lighter organic layer, which contains DPH, DMAE, hexane, and other byproducts, is pumped into a crystallizer at 6 bar with a 5M HCl solution in IPA. In the crystallizer, the mixture goes through three temperature zones. In the first zone, the mixture is heated to 50°C for 2 minutes, which allows the HCl to protonate the free-base DPH and ensures the mixture is completely dissolved. In the second zone, the mixture is cooled to 25°C over 5 minutes, which causes the mixture to become supersaturated and thereby induces nucleation. In the third zone, the mixture is cooled further to 5°C over 16 minutes to allow the nuclei to grow into crystals of the final product. After this step, the product has 95% purity. The mixture is then transferred into a filter and washed with hexane to remove residual free-base DPH, byproducts, HCl, IPA, and DMAE. Then, the DPH·HCl solution is recycled back into the crystallizer, and hexane is added to restore the mixture to its liquid fraction coming out of the decanter. After the second cycle through the crystallizer, the product has greater than 98% purity. The remaining purified DPH·HCl and hexane are screw fed into a dryer, where the hexane is evaporated off with nitrogen at 100°C. The vapor stream is then compressed to 20 bar and cooled to 27°C, which condenses the hexane from the nitrogen. The vapor-liquid mixture is then flashed, and each component is recycled back to its respective storage tank. The final dried product is screw fed into a final storage tank. Block 4 takes 2 hours and 16 minutes to complete.

Table 25. Simplified Block 4 Product Stream Table*

Name	**Crude DPH feed**	**Hexane feed**	**Decanter output**	**5M HCl/IPA feed**	**Crystallizer output**	**Hexane feed 2 (per wash)**	**Filter output**	**Dryer output**
Mass (kg)	1227.8	534.9	824.8	269	1093.8	264.2	374.2	249.5
Temperature (C)	25	25	25	25	5	25	25	70
Phase(s) of stream	l (org) :l (aq)	l	l (org)	l	(30) s:l (70)	l	(67) s:l (33)	s
Mass Compositions (kg)								
Free-base DPH	277.2	—	277.2	—	27.7	—	—	—
Hexane	—	535	535	—	535	264.2	124.7	—
Neutral Byproducts	7.9	—	7.9	—	7.9	—	—	—
H2O	820.8	—	—	—	—	—	—	—
HCl	—	—	—	41.5	41.5	—	—	—
Isopropanol	—	—	—	227.5	227.5	—	—	—
NaOH	53.7	—	—	—	—	—	—	—
DMAE	4.7	—	4.7	—	4.7	—	—	—
Purified DPH HCl	—	—	—	—	249.5	—	249.5	249.5
NaCl	63.5	—	—	—	—	—	—	—

*Full stream tables including waste streams can be found in the Appendix

2. Final Plant Schedule

The plant, which is located in Ponca City, Oklahoma, will run for a total of 7512 hours each year, producing 457,320 kg of DPH in 1,833 total batches. It will operate 313 days per year, which accounts for holidays and a week-long facility shut down for cleaning every six weeks. The plant will run for 24 hours each day. Each startup batch takes 9 hours and 52 minutes, and all subsequent batches take 4 hours and 4 minutes each. Each batch produces 250 kg of DPH.

VI. Economic Analysis

1. Fixed Capital Investment

The fixed capital investment (FCI) includes the cost of designing, constructing, and installing our plant. The cost of the equipment was estimated using Table 7.2 in Towler and Sinnott[23] or provided by Aspen for unit operations designed in Aspen. Table 26, lists the costs of all purchased equipment by equipment type and quantity in the whole process.

Table 26. Purchased Equipment Cost

Purchased Equipment		
Equipment Type	**Quantity**	**Cost**
Pumps/Blowers/Compressors	17	$137,237.00
Screw Feeders	10	$483,000.00
Reactors	3	$1,666,099.00
Tanks	24	$2,337,733.00
Filters	2	$361,750.00
Heat Exchangers	9	$8,959,696.00
Dryers	3	$2,905,862.00
Mixers and Separators	3	$1,790,240.00
Crystallizer	1	$243,623.00

Purchased equipment is about 20% of the FCI. The costs must be scaled to the current value of money because the table prices are from 2010. After accounting for inflation, the total cost of equipment is $35,425,093.00. Therefore, the total FCI is $177,125,466. The other 80% includes the necessary costs for building a new plant, which are listed below in Table 27.

Table 27. Total Capital Cost

Categories	**% of FCI**	**Cost**
Purchased Equipment	20	$35,425,093.00
Installation	9	$15,941,292.00
Instrumentation	7	$12,398,782.00
Piping	6	$10,627,528.00
Electrical Systems	4	$7,085,018.00
Buildings	12	$21,255,056.00
Yard Improvements	8	$14,170,037.00
Service Facilities	1	$1,771,254.00
Engineering and Supervision	12	$21,255,056.00
Construction	8	$14,170,037.00
Legal Expenses	1	$1,771,254.00
Contractors Fee	2	$3,542,509.00
Contingency	10	$17,712,546.00

2. Utilities, Waste Treatment, and Labor

Utility costs include steam, cooling water, chilled water, glycol, and electricity. The cost of the heating and cooling utilities are very low because they will be recycled. Table 28 shows the values for each utility cost, and Table 29 shows waste treatment costs. Costs were estimated using Turton Table 8.3[27]. Detailed calculations can be found in the Appendix. Labor costs are given in Table 30.

Table 28. Utility Cost per Year

Utility	**Cost USD/Year**
Chilled Water	$12,112.00
Cooled Water	$630.00
Glycol	$151,861.00
Steam	$26,457.00
Electricity	$109,554.00

Table 29. Waste Treatment Cost per Year

Waste Treatment	**Cost USD/Year**
Block 1	3,937,190.00
Block 2	6,670,656.00
Block 3	-
Block 4	21,947,059.00

Table 30. Labor Cost

Block	**Operators per Shift**	**Operators per Seat**	**Total Operators**	**Cost for Operators Salary**	**Supervisor Salary**
1	12	4	48	$2,400,000	$600,000
2	3	4	12	$600,000	$150,000
3	3	4	12	$600,000	$150,000
4	12	4	48	$2,400,000	$600,000
Total	30	-	120	$6,000,000	$1,500,000
	Total Labor Cost: $7,500,000				

3. Raw Materials

Bulk prices for most chemicals were found using the price indexes or from vendors online with publicly listed bulk prices. If a bulk price was not found, the lowest available price per kg was used. For this project, the delivery costs of raw materials were not included. Table 31 lists the annual raw material costs for this process. The total annual cost of the raw materials is $244,262,496.

Table 31. Cost of Raw Materials

Raw Material	Cost per kg	Quantity (kg) per batch	Quantity (kg) per year	Annual Cost
Benzophenone	$19.00	225	412,875	$32,131,242.00
Methanol	$0.48	19.11	6304	$3,025.00
Sodium Borohydride	$250.00	44.8	82,208	$84,180,096.00
DM Water	$0.01	2400	4,404,000	$60,129.00
37% Aq. Hydrogen Chloride	$0.22	463.6	850,706	$766,580.00
Nitrogen	$0.11	2400.45	4,404,826	$1,984,617.00
DMAE	$33.71	101.46	186,179	$25,706,622.00
IPA	$1.17	269.04	490,459	$573,838.00
Hexane	$28.65	1841.14	3,841,116	$96,695,584.00
NaOH	$0.32	898.3	1,648,381	$2,160,542.00

4. Overall Operational Cost

The overall cost of manufacturing for DPH-HCl was estimated using Equation 8.2 in Turton[24]. The operational cost was estimated to be $504,644,693. The wholesale price of packaged Benadryl was found to be $15,983 per kg[28]. Our plant is producing generic DPH powder so the price has to be reduced to account for lack of packaging and generic brand. That puts the wholesale price of our product to be $3356 per kg. Generic DPH is sold at 30% less than brand name Benadryl. Additionally, the active pharmaceutical ingredient (API) for small molecules typically accounts for 30% of the overall cost of packaged and formulated medication[29]. Therefore to get our price of $3356 per kg, we took the wholesale cost of Benadryl which accounted for packaging and reduced it by 30% to reflect the cost for generic DPH including packaging and formulation. Then to get the cost of DPH without packaging, we reduced the value by 70% since only 30% of that cost is attributed to API to get our wholesale price. Our plant produces 457,320 kg of DPH per year therefore if we sell all of our product, our annual revenue would be $1.5 billion. To calculate the actual profit of the plant, the cost of manufacturing, expenses, taxes, and depreciation were all subtracted from the annual revenue. A straight depreciation of 25% was assumed for our product. Our plant will take a year and a half to build, and we will allow another six months to troubleshoot. Thus, in the first year, we will only sell 6 months worth of product. After the first two years, we will be running at full capacity with a net annual profit of $638 million. Figure 16 shows the total profit we will make each year after taxes and expenses are taken out. Our plant is very profitable and is an economic go. Figure 17 demonstrates that even if we only sell 75% of our product each year due to external factors like market competition, we still make a net annual profit of $254 million.

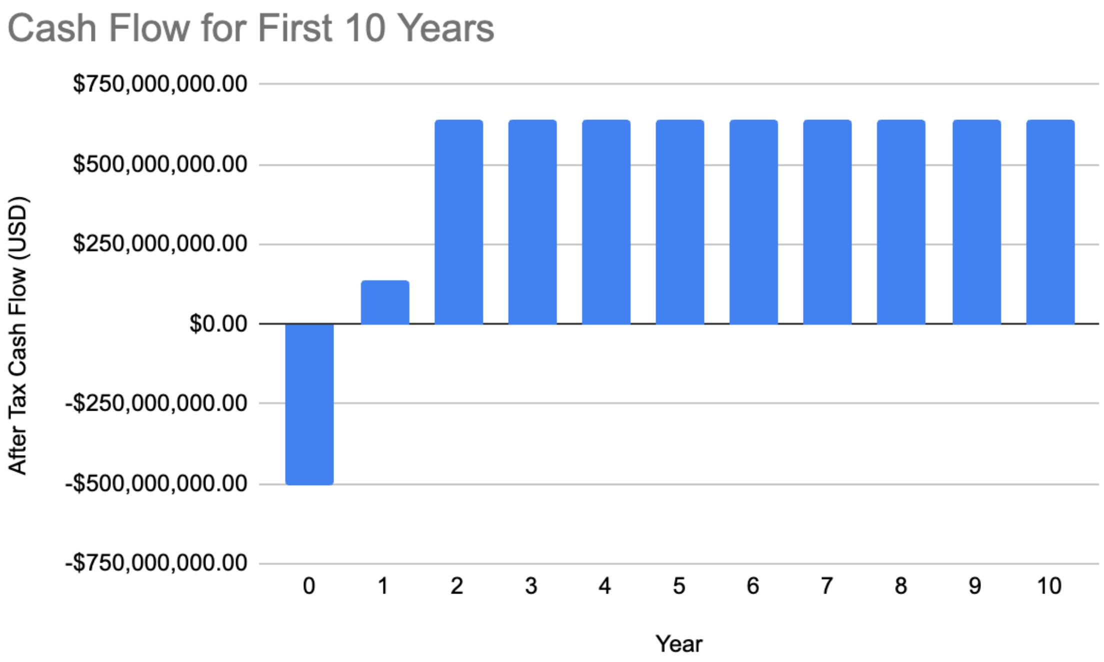


Figure 16. Cash Flow during the first 10 years

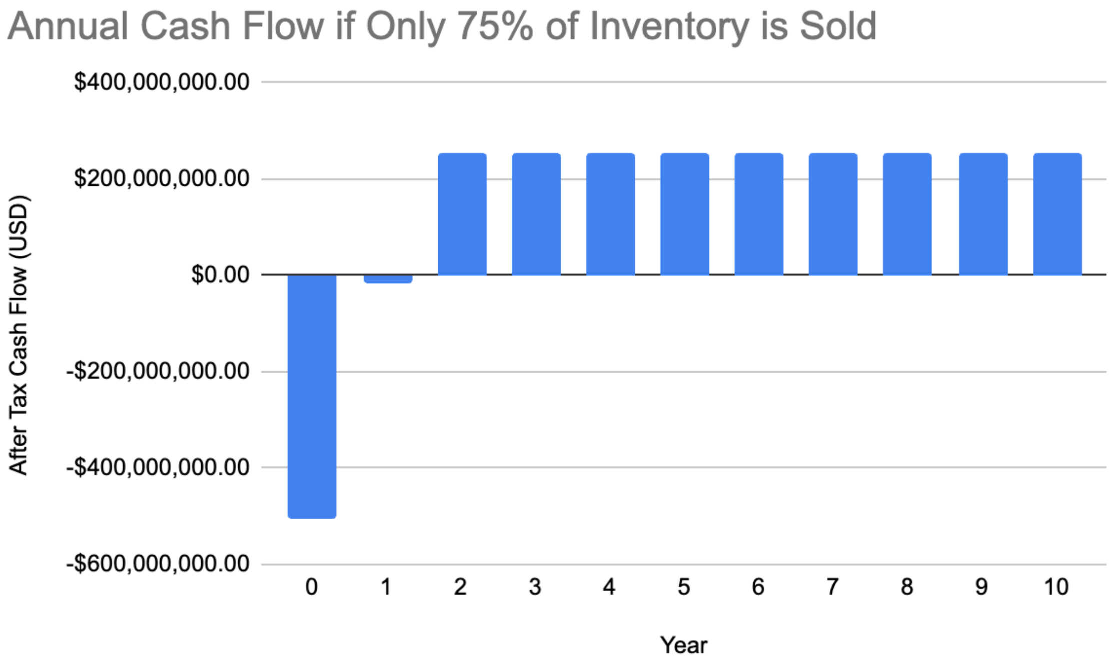


Figure 17. Cash Flow if only 75% of Inventory Sells

5. Social and Ethical Considerations

A strong safety culture is reinforced by documented SDS awareness training and mandatory refreshers on chemical safety, cGMP principles, and emergency response. Competitive wages, benefits, and a commitment to transparency ensure employee welfare. Local communities benefit from minimal noise as all our operations are indoors, minimal traffic congestion as our plant is in a rural location, and minimal odors since only water vapor is vented to the atmosphere. We will also keep open communication channels with the community to address concerns.

Procuring raw materials from ethically certified suppliers supports responsible sourcing, and eliminating bromine-based processes further reduces ecological impact. Public health efforts focus on transparent labeling, social media engagement, and potential cost reductions through greener processes helping to make Diphenhydramine more affordable and environmentally responsible.

VII. Conclusion and Recommendations

In conclusion, our team successfully designed a batch manufacturing plant for the production of Diphenhydramine Hydrochloride (DPH·HCl), which utilizes an alternative process significantly reducing hazardous waste and maintaining product purity above 98%. The plant's innovative approach removed corrosive bromine, demonstrating improved environmental sustainability, enhanced operational safety, and considerable economic viability.

From an economic standpoint, we highly recommend that this plant be built using the equipment and procedure outlined in this report. This process would yield an annual profit of roughly $638 million per year at an operating schedule of 313 days per year. Even if we were to only sell 75% of our product due to competition in the market, we would still make a profit of approximately $254 million per year. We could even lower the price of our product to improve accessibility.

Recommendations for Future Work

Further experiments should be run to determine solubility of the compounds, particle size, ideal filter material, and vacuum pressure for the filters proposed as each of the filters is assumed to give perfect separation. A similar assumption was made for the reactors as kinetic data was either unavailable for our reactions or available with differing solvents. For R-101 and R-201 kinetic data was estimated using a similar reaction but not exact with the solvents we were using, and with R-301 there was no kinetic data at all and a 100% conversion of CDPM was assumed. Experiments to determine the reaction rate for each reactor would aid in creating a more accurate model, which could be used to design equipment that would guarantee more accurate yield and purity.

Lab-scale testing can also be conducted to determine mixture property data such as heat capacity, viscosity, and thermal conductivity as these properties were estimated from Aspen V14. More precise data on each mixture would allow for more exact mixing, heating, and cooling calculations and design. After a reliable library of property data is assembled, a pilot run of the process will create an exact plant schedule, since the current schedule assumes process times for certain pieces of equipment, washing, reactions, and separations.

There will also be additional costs that we did not account for such as maintenance and raw material delivery.

Finally it is recommended for future teams to address the best way to manage the hydrogen produced in R-101. Our current plant design purifies the hydrogen produced and then removes it from the plant; however, this hydrogen could be utilized in a fuel cell for sustainable energy recovery and usage in the plant.

VIII. Acknowledgments

We would like to thank Shannon McCulloughm, Ron Unnerstall, and Eric Anderson for assisting and mentoring us throughout the design of this process facility.

IX. References

(1) *Diphenhydramine Market Size | Mordor Intelligence*. https://www.mordorintelligence.com/industry-reports/diphenhydramine-market (accessed 2025-01-21).
(2) *Diphenhydramine Hydrochloride Market Size, Share & Forecast to 2034*. https://www.chemanalyst.com/industry-report/diphenhydramine-hydrochloride-market-4191 (accessed 2025-05-06).
(3) *Diphenhydramine hydrochloride | Histamine H1-Receptor Antagonist | MedChemExpress*. MedchemExpress.com. https://www.medchemexpress.com/Diphenhydramine-hydrochloride.html (accessed 2025-01-21).
(4) Sonavane, S.; Pagire, R.; Patil, D.; Pujari, U.; Nikam, R.; Pradhan, N. Improved, Solvent Free, Atom Efficient Commercial Process for the Synthesis of Diphenhydramine Hydrochloride. *CGC* **2018**, *4* (3). https://doi.org/10.2174/2213346105666171227152717.
(5) Snead, D. R.; Jamison, T. F. End-to-End Continuous Flow Synthesis and Purification of Diphenhydramine Hydrochloride Featuring Atom Economy, in-Line Separation, and Flow of Molten Ammonium Salts. *Chem. Sci.* **2013**, *4* (7), 2822–2827. https://doi.org/10.1039/C3SC50859E.
(6) Bromine Safety Data Sheet. https://www.sigmaaldrich.com/DE/de/sds/aldrich/470864?srsltid=AfmBOorW7M-4wFYpppw1bFphdIzvmYZ5Ysc7M-jcvZaqu1cOdJRLZHTN.
(7) Research, C. for D. E. and. MOU 225-24-020. *FDA* **2024**.
(8) Diphenhydramine Hydrochloride. https://doi.org/10.31003/USPNF_M27130_04_01.
(9) *Diphenhydramine Hydrochloride, USP*. https://www.spectrumchemical.com/diphenhydramine-hydrochloride-usp-di160 (accessed 2025-04-01).
(10) Burton, I. W.; Quilliam, M. A.; Walter, J. A. Quantitative^1 H NMR with External Standards: Use in Preparation of Calibration Solutions for Algal Toxins and Other Natural Products. *Anal. Chem.* **2005**, *77* (10), 3123–3131. https://doi.org/10.1021/ac048385h.
(11) Bhal, S. *The Basics of Interpreting a Proton (1H) NMR Spectrum*. ACD/Labs. https://www.acdlabs.com/blog/the-basics-of-interpreting-a-proton-nmr-spectrum/ (accessed 2025-04-04).
(12) Lo, C. F.; Karan, K.; Davis, B. R. Kinetic Studies of Reaction between Sodium Borohydride and Methanol, Water, and Their Mixtures. *Ind. Eng. Chem. Res.* **2007**, *46* (17), 5478–5484. https://doi.org/10.1021/ie0608861.
(13) *Diphenhydramine Hydrochloride Market Size, Share & Forecast to 2034*. https://www.chemanalyst.com/industry-report/diphenhydramine-hydrochloride-market-4191 (accessed 2025-01-21).
(14) Brown, H. C.; Wheeler, O. H.; Ichikawa, K. Chemical Effects of Steric Strains—XIII: Kinetics of the Reaction of Sodium Borohydride with Carbonyl Groups—a Convenient Tool for Investigating the Reactivities of Aldehydes and Ketones. *Tetrahedron* **1957**, *1* (3), 214–220. https://doi.org/10.1016/0040-4020(57)88041-7.
(15) Konkol, J. A.; Singh, R.; Muzzio, F. J.; Tsilomelekis, G. On the Synthesis of Diphenhydramine: Steady State Kinetics, Solvation Effects, and in-Situ Raman and Benchtop NMR as PAT. *Chemical Engineering Journal* **2024**, *493*, 152159. https://doi.org/10.1016/j.cej.2024.152159.
(16) *763: Phase diagram of water*. https://webhome.phy.duke.edu/~hsg/763/table-images/water-phase-diagram.html (accessed 2025-05-05).
(17) Chilton, T. H.; Drew, T. B.; Jebens, R. H. Heat Transfer Coefficients in Agitated Vessels.
(18) Marinos-Kouris, D.; Krokida, M.; Mujumdar, A. Rotary Drying. In *Handbook of Industrial*

Drying, Third Edition; Mujumdar, A., Ed.; CRC Press, 2006. https://doi.org/10.1201/9781420017618.ch7.
(19) Alloy Selection for Service in Caustic Soda: A Guide to the Use of Nickel-Containing Alloys 2nd Ed, 2019.
(20) *Calculate sedimentation velocity online*. https://www.peacesoftware.de/einigewerte/sedimentationsgeschwindigkeit_e.html (accessed 2025-02-27).
(21) *Fundamentals of Momentum, Heat, and Mass Transfer, 7th Edition | Wiley*. Wiley.com. https://www.wiley.com/en-us/Fundamentals+of+Momentum%2C+Heat%2C+and+Mass+Transfer%2C+7th+Edition-p-9781119495413R150 (accessed 2025-03-23).
(22) Anderson, E. How To Design a Pump for CHE 4476.
(23) *Chemical Engineering Design: Principles, Practice and Economics of Plant and Process Design (Table 7.2)*; Towler, G., Sinnott, R., Eds.; Elsevier/Butterworth-Heinemann: Amsterdam Boston, 2008.
(24) Food and Drug Administration. PART 210—CURRENT GOOD MANUFACTURING PRACTICE IN MANUFACTURING, PROCESSING, PACKING, OR HOLDING OF DRUGS; GENERAL.
(25) Food and Drug Administration. *PART 211—CURRENT GOOD MANUFACTURING PRACTICE FOR FINISHED PHARMACEUTICALS*.
(26) *Ponca City Climate, Weather By Month, Average Temperature (Oklahoma, United States) - Weather Spark*. https://weatherspark.com/y/8252/Average-Weather-in-Ponca-City-Oklahoma-United-States-Year-Round (accessed 2025-04-29).
(27) *Analysis, Synthesis, and Design of Chemical Processes*, 4th ed.; Turton, R., Ed.; Prentice Hall: Upper Saddle River, NJ, 2012.
(28) *CVS Health Allergy Relief Diphenhydramine Tablets, 24 Count*. CVS Pharmacy. https://www.cvs.com/shop/cvs-health-allergy-relief-diphenhydramine-tablets-prodid-1011700?skuId=477066 (accessed 2025-04-30).
(29) *Getting a Grip on COGS in Generic Drugs*. BCG Global. https://www.bcg.com/publications/2019/getting-a-grip-on-cogs-in-generic-drugs (accessed 2025-04-30).
(30) *CheCalc - Blower & Fan Calculations*. https://checalc.com/fan.html (accessed 2025-05-06).

SDS Hyperlinks

(1) Benzophenone: www.sigmaaldrich.com/US/fr/sds/sial/b9300?
gustavus.edu/academics/departments/chemistry/documents/documents/benzophenone.pdf
(2) Sodium Borohydride: www.sigmaaldrich.com/US/en/sds/aldrich/452882?srsltid=AfmBOor5sw8nS806kzsDFzeBut6KQ2ggaT3p3uFjL9b26oyqJ9k-TVeU
(3) Methanol: https://www.sigmaaldrich.com/US/en/sds/sial/322415?
(4) Hydrogen: https://dept.harpercollege.edu/chemistry/sds/Hydrogen%20Gas.pdf
www.sigmaaldrich.com/US/en/sds/aldrich/295396?srsltid=AfmBOorruUdFgfVhmLuR1i8ze_U_5pow7Do6-gvZ793UXvsvMlZy2kx8
(5) Sodium Tetramethoxyborate: www.biosynth.com/Files/MSDS/TA/A0/MSDS_TAA02469_4000_EN.pdf
(6) Hydrogen Chloride: www.sigmaaldrich.com/US/en/sds/SIGMA/H1758?
(7) Chlorodiphenylmethane: www.fishersci.com/store/msds?partNumber=AC154660500&countryCode=US&language=en

www.sigmaaldrich.com/US/en/sds/aldrich/125032?userType= anonymous

(8) Dimethylaminoethanol: www.sigmaaldrich.com/US/en/sds/aldrich/471453?
www.fishersci.com/store/msds?partNumber=AC116182500&countryCode=US&language=en

(9) Sodium Hydroxide: www.fishersci.com/content/dam/fishersci/en_US/documents/programs/education/regulatory-documents/sds/chemicals/chemicals-s/S25550.pdf
www.sigmaaldrich.com/US/en/sds/sigald/s8045?

(10) Diphenhydramine: www.tcichemicals.com/US/en/p/D4744#docomentsSectionPDP
cdn.pfizer.com/pfizercom/products/material_safety_data/PD016.pdf

(11) Diphenhydramine Hydrochloride: www.fishersci.com/store/msds?partNumber=AC350850250&productDescription=DIPHENHYDRAMINE+HYDROCHLO+25GR&vendorId=VN00032119&countryCode=US&language=en
www.sigmaaldrich.com/US/en/sds/sigma/d3630?

(12) Hexane: https://www.airgas.com/msds/001060.pdf
www.sigmaaldrich.com/US/en/sds/sial/296090?srsltid=AfmBOooPcq4_qJWQg3UOwN3TYPW8tL3T9TMM8yu_qXNXPBVs1iJqpvl1

(13) Isopropanol: www.sigmaaldrich.com/US/en/sds/SIAL/W292912?

X. Appendix

R-101

The density of the mixture: $\rho = \frac{M_{total}}{V_{total}}$

Density of mixture = 771.1 kg/m^3

Impeller Power

Re (assume turbulent and low viscosity) = 10,000

Marine propeller : due to low viscosity and low power usage

Diameter = 0.8 m

Height = 1.6 m (2L to 1 D ratio)

0.26 m impeller diameter ratio (3 diameter to 1 impeller)

0.53 m above the ground level (⅓ of height)

Impeller Reynolds number: Re= (N*d^2*ρ) / μ

N = 10,000*(0.000547 Pa-s) / (0.26 m)^2 * 771.0 kg/m^3

N > 1 Rotations per second, will assume 4 to make it industry standard

4 Rotations/s = 240 Rotations/min

Calculate power = P = np * density* rps^3*D^5 - assume a power number of 0.5

P=0.5* 771.0 g/m^3*(4 rot/s)^3*(0.26 m)^5

P = 29.3 watts

Mixing and Heat transfer

Viscosity (μ), Heat Capacity (Cp), and thermal conductivity (k) of mixture estimated using Aspen Plus 14.

Viscosity = 1.32324 lb/ hr-ft = 0.547 cP

Heat Capacity = 0.5921 BTU/ lb-F = 2479.03 J/kg-K

Thermal conductivity = 0.113 BTU/hr-ft-F = 0.196 W/m-K

Mixing Heat transfer coefficient correlation[8]:

$$\frac{\frac{hD}{k}\left(\frac{\mu_j}{\mu}\right)^{0.14}}{\left(\frac{C_p\mu}{k}\right)^{1/3}} = 0.87Re^{0.62}$$

-μj/μ = viscosity at wall surface/ viscosity of mixture = assume 1

h_j =[(262.73)*[(Cp)*(μ) / (k)]^(⅓)]/ (1^0.14) * [(k)/(D)]

h_j =[(262.73)*[(0.5921 BTU/ lb-F)(1.32324 lb/ hr-ft) / (0.113 BTU/hr-ft-F)]^(⅓)]/ (1^0.14) * [(0.113 btu/hr-ft-F)/(2.62467 ft)]

Heat coefficient of mixture with turbulent flow: h = 21.6 BTU/hr-ft^2-F = 122.65 W/m^2-k

Heat Duty Q= -61.6566 KW - estimated using Aspen Plus 14

Propylene Glycol Cooling Coil

Heat Transfer EQ: Q = UA(T_{mix}- T_{cool})

Assume negligible wall resistance (U= h)

Coil Dimensions:

T_{cool} = -30 C

Coil SA = A = Q/ (h*(T_{mix}- T_{cool})) = (61.65 KW)/ ((0.122KW/m^2-K)*(300.15K-243.15K))

Coil Surface area = 8.819 m^2

Tube length = L = A/(2π*0.01m) = 140.36 m

C of coil = C = 2π*(reactor diameter) = 2π*(0.8m) = 5.02m

Coil height = H = L/C * (0.01m*2) = 0.5584m

Liquid height = (liquid vol)/ π*(d/2) = (0.702 m^3)/ π*(0.8/2) = 1.397 m

Mass of P. Glycol in Coil: Q = m(Cp)dt

Cp P. Glycol = 2369.5 J/kg-K

Q = m (Cp)dt

Mass of glycol= m =(61.6566 kj/s)/[(2369.5 J/kg-K)*(300.15 K) - (2369.5 J/kg-K)*(243.15 K)]

m= 1643.4 kg/h

R-201

R-201: Impeller Power

The density of the mixture: $\rho = \frac{M_{total}}{V_{total}}$

Density of mixture = 1093.8 kg/m^3

Re (assume turbulent and low viscosity) = 10,000

Marine propeller : due to low viscosity and low power usage

Tank Diameter = 0.76 m

Tank Height = 1.52 m (2L to 1 D ratio)

0.253 m impeller diameter ratio (3 diameter to 1 impeller)

0.507 m above the ground level (⅓ of height)

Impeller Reynolds number: Re= (N*d^2*ρ) / μ

N = 10,000*(0.001 Pa-s) / (0.253 m)^2 * 865.48 kg/m^3

N > 1 Rotations per second, will assume 4 to make it industry standard

4 Rotations/s = 240 Rotations/min

Calculate power = P = np * density* rps^3*D^5 - assume a power number of 0.5

P = 0.5* 865.48 kg/m^3*(4 rot/s)^3*(0.253 m)^5

P = 28.898 watts = 29 watts

R-201: Mixing and Heat transfer

Viscosity (μ), Heat Capacity (Cp), and thermal conductivity (k) of mixture estimated using Aspen Plus 14.

Viscosity = 2.419 lb/ hr-ft = 1 cP

Heat Capacity = 0.76 BTU/ lb-F = 3178.49 J/kg-K

Thermal conductivity = 0.10858 btu/hr-ft-F = 0.188 W/m-K

Mixing Heat transfer coefficient correlation[8]:

$$\frac{\frac{hD}{k}\left(\frac{\mu_j}{\mu}\right)^{0.14}}{\left(\frac{C_p\mu}{k}\right)^{1/3}} = 0.87Re^{0.62}$$

-μj/μ = viscosity at wall surface/ viscosity of mixture = assume 1

h =[(262.73)*[(Cp)*(μ) / (k)]^(⅓)]/ (1^0.14) * [(k)/(D)]

h = [(262.73)*[(0.76 BTU/ lb-F)(2.419 lb/ hr-ft) / (0.10858 btu/hr-ft-F)]^(⅓)]/ (1^0.14)* [(0.10858 btu/hr-ft-F)/(2.493 ft)]

Heat coefficient of mixture with turbulent flow: = 29.375 btu/hr-ft2-F) = 166.689 (W/m^2-k)

Heat Duty Q= -93.91 KW - estimated using Aspen Plus 14

R-201: Chilled Water Cooling Coil

Heat Transfer EQ: Q = UA(T_{mix}- T_{cool})

Assume negligible wall resistance (U= h)

Coil Dimensions:

T_{cool} = 10 C

Coil SA = A = Q/(h*(T_{mix}- T_{cool})) = (93.91 KW)/((0.167KW/m^2-K)*(336.15K-283.15 K))

Coil Surface area = 7.718 m^2

Tube length = L = A/(2π*0.01m) = 122.83 m

C of coil = C = 2π*(reactor diameter) = 2π*(0.76m) = 4.775m

Coil height = H = L/C * (0.01m^2) = 0.5144m

Liquid height = (liquid vol)/ π*(d/2) = (0.702 m^3)/ π*(0.8/2) = 1.349 m

Mass of Chilled Water in Coil: Q = m(Hin-Hout)

Hin (10C) = 42.02 kj/kg

Hout (83C) = 347.61 kj/kg

Mass of cooling water = m =(-93.91 kj/s)/[42.02 kj/kg - 347.61 kj/kg]

m= 1106.3 kg/h

R-301

R-301: Impeller Power

The density of the mixture: $\rho = \dfrac{M_{total}}{V_{total}}$

Density of mixture = 994.134 kg/m^3

Re (assume turbulent and low viscosity) = 10,000

Marine propeller : due to low viscosity and low power usage

Tank Diameter = 0.62 m

Tank Height = 1.24 m (2L to 1 D ratio)

0.21 m impeller diameter ratio (3 diameter to 1 impeller)

0.413 m above the ground level (⅓ of height)

Impeller Reynolds number: Re= (N*d^2*ρ) / μ

N = 10,000*(0.01023 Pa-s) / (0.21 m)^2 * 994.13 kg/m^3

N > 1 Rotations per second, will assume 4 to make it industry standard

4 Rotations/s = 240 Rotations/min

Calculate power = P = np * density* rps^3*D^5 - assume a power number of 0.5

P = 0.5* 994.13kg/m^3*(4 rot/s)^3*(0.21 m)^5

P = 12.9 watts = 13 W

R-301: Mixing and Heat transfer

Viscosity (μ), Heat Capacity (Cp), and thermal conductivity (k) of mixture estimated using Aspen Plus 14.

Viscosity = 24.7427 lb/ hr-ft = 10.23 cP

Heat Capacity = 0.557668 BTU/ lb-F = 2333.29 J/kg-K

Thermal conductivity = 0.0736 btu/hr-ft-F = 0.127 W/m-K

Mixing Heat transfer coefficient correlation[8]:

$$\frac{\frac{hD}{k}\left(\frac{\mu_j}{\mu}\right)^{0.14}}{\left(\frac{C_p\mu}{k}\right)^{1/3}} = 0.87Re^{0.62}$$

-μj/μ = viscosity at wall surface/ viscosity of mixture = assume 1

h=[(262.73)*[(Cp)*(μ) / (k)]^(⅓)]/ (1^0.14) * [(k)/(D)]

h= [(262.73)*[(0.557668 BTU/ lb-F)(24.7427 lb/ hr-ft) / (0.0736 btu/hr-ft-F)]^(⅓)]/ (1^0.14)* [(0.0736 btu/hr-ft-F)/(2.03 ft)]

Heat coefficient of mixture with turbulent flow: = 54.42 (btu/hr-ft2-F) = 308.82 (W/m^2-k)

Heat Duty Q= 38.935 KW - estimated using Aspen Plus 14

R-301: Steam Heating Coil

Heat Transfer EQ: Q = UA(T_{mix}- T_{Heatl})

Assume negligible wall resistance (U= h)

Coil Dimensions:

Steam P = 15 bar

Coil SA = A = Q/(h*(T_{mix}- T_{cool})) = (38.935 KW)/((0.309KW/m^2-K)*(198 C- 160C)

Coil Surface area = 5.48 m^2

Tube length = L = A/(2π*0.02m) = 43.62 m

C of coil = C = 2π*(reactor diameter) = 2π*(0.62m) = 3.896m

Coil height = H = L/C * (0.02m^2) = 0.4479m

Liquid height = (liquid vol)/ π*(d/2) = (0.374 m^3)/ π*(0.62/2) = 1.24 m

Mass of Steam in Coil: -Q = m(-H)

H = H1- Hv

Hv = 844.56 kj/kg (T = 198C, P = 15 bar)

Tin = 198 C = 471.15K (vapor at 15 bar)

Tout= 175 C = 448.15K (175 C is temperature of reaction- liquid at 10 bar[16])

Cp = 4.4871 J/g-K

H1 = $\int_{471.15K}^{448.15K} C_p dt$ = -103.2 kJ/kg

H = -103.2 kJ/kg - 844.56 kj/kg = -947.7633 kj/kg

Mass of steam = m =(-38.935 kj/s)/ (-947.7633 kj/kg)

m = 0.04108 kg/s = 147.89 kg/h

Rotary Dryers

DR-101

Specific Heat Capacity of Solid

Cp_solid = (x_benzo * cp_benzo)+(x_benzhy * cp_benzhy)+(x_NaBH4 * cp_NaBH4)

Cp_solid = 0.652 kj/kg-k

Heat to dry solid from inlet temp to final temp

Q1 = total_mass_flowrate * cp_solid * (T_finaltemp - T_initial)

Q1 =619.5 kg/hr *0.652 kj/kgk *((273K+68)-(273K+27)) = 16562.36 kj/hr

Heating Moisture to vaporization temperature

Q2 = total_mass_flowrate * cp_moisture *(T_vap - T_inital)

Q2 =619.5 kg/hr * 0.837 kj/kg-k *((273K+65)-(273K+27)) =19713.94 kj/hr

Heat to evaporate moisture: [Q3 = methanol_flowrate * hvap_methanol]

Q3 = 200.8681818 kg/hr * 1160 kj/kg = 233007.1 kj/hr

Heat residual moisture to final temp
Q4 = total_mass_flowrate * 0.01 * cp_solid * (T_final - T_initial)
Q4=418.6318182 kg/hr *0.01*2.53 kj/kgk *((273K+68)-(273K+27)) = 434.25 kj/hr

Q_total = (Q1 + Q2 + Q3 + Q4) * 0.9 = 242745.87 kj/hr - Assume 0.9 to account for heat loss.

T_air_2 = (120-65)/EXP(2)+65 = 83.27 K - Assume NTU of 2 (rotary dryer)
M_air = Q/(cp_air * (T_air_2 - T_air_1) = 2400 kg/hr
T_lm = (473-(273+65))-((273+83.27)-(273+65))/ ln((473-(273+65))/((273+83.27)-(273+65)))
T_lm = 125.86 K

Total drying time:

$$\tau = \frac{0.3344L}{SN^{0.9}D} + \frac{0.608BLG}{F}$$

Dryer diameter = D = sqrt(4*m_a / (pi * 515 kg/hrm^2) = 2.44 m
Heat transfer coefficient = Ua = 4*515^0.67 *1/D = 107.72 kj/(hrm^3k)
Dryer length = L = 4 * Q / (pi * d^2 *Ua * T_lm) = 3.84 m
Rpm = N = 0.5/(pi*d) * 60 = 3.92 RPM
Particle diameter = B =5*4000 µm^-0.5 - Assume particle diameter to be 4000 µm
Dryer angle = S = 2°
Gas Mass Velocity = G = 515 kh/hrm^2
F = m_feed = 619.5 kg/hr
Total drying time = 16.45 min

DR-102

Specific Heat Capacity of Solid
Cp_solid = x_benzhydrol * cp_benzhydrol = 0.67 kj/kgk

Heat to dry solid from inlet temp to final temp
Q1 = total_mass_flowrate * cp_solid * (T_finaltemp - T_initial)
Q1 =327.28 kg/hr * 0.83 kj/kgk *((273K+68)-(273 K+50)) = 4870.62 kj/hr

Heating Moisture to vaporization temperature
Q2 = total_mass_flowrate * cp_moisture *(T_vap - T_inital)
Q2 =327.28 kg/hr 1.38 kj/kgk *((273K+100)-(273 K+50)) =19713.94 kj/hr

Heat to evaporate moisture: [Q3 = water_flowrate * hvap_water]
Q3 = 105.78 kg/hr * 2260 kj/kg = 239081 kj/hr

Heat residual moisture to final temp
Q4 = total_mass_flowrate * 0.01 * cp_solid * (T_finaltemp - T_initial)
Q4 =221.49 kg/hr *0.01*4.18 kj/kgk *((273K+100)-(273 K+50)) = 462.92 kj/hr

Q_total = (Q1 + Q2 + Q3 + Q4) * 0.9 = 240288.5 kj/hr - Assume 0.9 to account for heat loss.

T_air_2 = (120-100)/EXP(2)+100 = 102.7067057 K - Assuming a NTU of 2 (rotary dryer)
M_air = 240288.5 kj/hr /(1.04 kj/kgk*((200K+273)-(373K))) = 2310.47 kg/hr
T_lm=((273+120)-(273+100))-((273+102.71-(273+100))/ln(((273+120)-(273+100))/((273+102.71)-(273+100))) K = 18.65 K

Total drying time:

$$\tau = \frac{0.3344L}{SN^{0.9}D} + \frac{0.608BLG}{F}$$

Dryer diameter = D = sqrt(4*m_a / (pi * 515 kg/hrm^2) = 2.43 m
Heat transfer coefficient =Ua = 4*515^0.67 *1/D = 106.06 kj/hrm^3k
Dryer length = L = 4 * Q / (pi * d^2 *Ua * T_lm) = 26.29 m
RPM = N = 0.5/(pi*d) * 60= 3.94 RPM
Particle diameter = B=5*4000^-0.5 - Assume particle diameter to be 4000µm
Dryer angle = S = 2°
Gas Mass Velocity = G = 2310.47 kg/hr / 4.5m^2 = 515kg/hrm^2
F = m_feed = 327.28 kg/hr
Total drying time = 28.17 min

DR-401

Specific Heat Capacity of Solid
Cp_solid = x_DPH * cp_DPH = 0.9 kj/kgk

Heat to dry solid from inlet temp to final temp
Q1 = total_mass_flowrate * cp_solid * (T_finaltemp - T_initial)
Q1 =374.2 kg/hr * 0.9 kj/kgk *((273K+70)-(273K+25)) = 15155.1 kj/hr

Heating Moisture to vaporization temperature
Q2 = total_mass_flowrate * cp_moisture *(T_vap - T_inital)
Q2 =327.28 kg/hr 0.75 kj/kgk *((273K+70)-(273K+25)) =12685.38 kj/hr

Heat to evaporate moisture: [Q3 = hexane_flowrate * hvap_hexane]

Q3 = 248.2 kg/hr * 520 kj/kg = 129067.5 kj/hr

Heat residual moisture to final temp
Q4 = total_mass_flowrate * 0.01 * cp_solid * (T_finaltemp - T_initial)
Q4 =125.99 kg/hr *0.01*1.35 kj/kg-k *((273K+70)-(273K+25)) = 76.54 kj/hr

Q_total = (Q1 + Q2 + Q3 + Q4) * 0.9 = 172682.97 kj/hr   - Assume 0.9 to account for heat loss.

T_air_2 = (200-70)/EXP(2)+70 = 87.59 K   - Assume NTU of 2 (rotary dryer)
M_air =205855.8 kj/hr /(1.04 kj/kg-k*((200K+273)-(373K))) = 1660.41 kg/hr
T_lm =((273+200)-(273+70))-((273+87.59)-(273+200))/
ln(((273+200)-(273+70))/((273+87.59)-(273+70))) K = 186.2 K

Total drying time: $\tau = \frac{0.3344L}{SN^{0.9}D} + \frac{0.608BLG}{F}$
Dryer diameter = D = sqrt(4*m_a / (pi * 515 kg/hrm^2) = 2.02 m
Heat transfer coefficient = Ua = 4*515^0.67 *1/D = 1118.62 kj/hrm^3k
Dryer length = L = 4 * Q / (pi * d^2 *Ua * T_lm) = 9.62 m
Rpm = N = 0.5/(pi*d) * 60= 4.71 RPM
Particle diameter = B =5*4000^-0.5 - Assume particle diameter to be 4000µm
Dryer angle = S = 2°
G = 1660.41 kg/hr / 3.224103339 m^2 = 515 kg/hrm^2
F = m_feed = 374.2
Total drying time =10.63 min

Mixers and Separators

DC-201

Density organic phase: 1193 kg/m^3
Density aqueous phase: 1180 kg/m^3

Decanter Dimensions
Liquid Volume = V_l = .1989 (1800) = 358.02 L
Decanter volume = 411.72 L ~ 415 L - assume additional 15% from V_l for buffer
V = pi r^2 L → .415 = Πr^2 (6r)   -L/D ratio of 3 to 1
Decanter radius = R = 0.28 m
Decanter Diameter = D = 0.56
Decanter Length = L = 1.68 m

Residence Time
Particle Diameter = dp = 2.5 x 10^-9 m
Setting Velocity = V = $(\rho_p - \rho_f)$ gd^2 /18 μ = (1193 - 1178.8) (9.81)(2.5 x 10^-9) / 18(.0004) =
Setting Velocity = V = 0.000049 m/s
From settling velocity assume residence time of 30 min

DC-401

Density organic phase (kg/m^3): 750 kg/m^2
Density aqueous phase (kg/m^3) : 1,110 kg/m^3

Decanter Dimensions
Liquid Volume = V_l = 1959.28 L
Decanter volume = 2356.19 L - assume additional 15% from V_l for buffer
V = pi r^2 L - L/D ratio of 3 to 1
Decanter radius = R = 0.49 m
Decanter Diameter = D = 1 m
Decanter Length = L = 3 m

Residence Time
Particle Diameter = dp = 2.5 x 10^-9 m
Settling Velocity = V = $(\rho_p - \rho_f)$ gdp^2 /18 μ = (1,110 kg/m^3 - 750 kg/m^2)*(9.81 m/s^2)(2.5 x 10^-9 m) / 18 (0.00085 Pa/s) = 0.000577 m/s
From settling velocity assume residence time of 20 min

F-101

Dimensions:
Total liquid mass = M = 800 kg *3 + 435.16 kg = 2835.16 kg/hr
Total liquid volume = V = 2.42 m^3 + 0.34 m^3 = 2.76 m^3
Filter Volume = 3 m^3
Filter D = 1.96 m
Filter H = 3.92 m

Estimating time per wash cycle
Assume filtration rate of 150 L/ m^2-h
Filter Area = 12.08 m^2
Flux = filtration rate * A = 150 L/ m^2-h * 12.08 m^2 = 1812 L/h
Time to filter 800L = (800/1812) h = 0.44 h *3 = 1.32 h

F-401

Dimensions:
Total liquid mass = M = 1093.81 kg + 264.24 kg = 1358.05 kg
Total liquid Volume = V = (0.4 m^3)*2 + 1.38 m^3 = 2.18 m^3
Filter Volume = 2.5 m^3
Filter D = 1.85 m
Filter H = 3.7m

Estimating time per wash cycle
Assume filtration rate of 150 L/ m^2-h
Filter Area = 10.75 m^2
Flux = filtration rate * A = 150 L/ m^2-h * 10.75 m^2 = 1612.5 L/h
Time to filter 400 L = (400/1612.5) h = 0.248 h *2 = 0.496 h

M-301

1150 L Feed
15% safety so 1350 L mixer
Dimensions**:** 2:1 ratio
V = pi D^2/4 H = pi D^2/4 (2D)
D = 0.951 m and H = 1.9 m
Impeller ⅓ of height = 0.63m
Impeller width = 0.315 m
Re = ND^2p / μ
N = impeller rotational speed = 300 rpm = 5 rps
D = impeller diameter = 0.315 m
ρ = fluid density = m/v = .3388 kg/s / .000281 m^3/s = 1205.69 kg/m^3
μ = dynamic viscosity (Pa s) = .00101 Pa s
RE = 5(0.315^2)(1205.69)/.00101 = 592250.45 therefore Turbulent Flow

$P_i = P_n * n^3 * p * d_b^5$ - pitch blade turbine

$P_i = P_n * n^3 * p * d_b^5$ = 1.27 (5)^3 rps (1205.69 kg/m^3) (0.315^5 m) = 593.6 watts

Crystallizer

Stoichiometric balance for required amount of 5M HCl/IPA

Mols Free DMAE = 52.6 mol/h

Mols Free DPH = 1085.6 mol/h

Moles of HCl needed = (52.6 mol/h) + (1085.6 mol/h) = 1138.2 mol/h *(36.46 g/mol)*(10^-3)

Mass of HCl needed = 41.5 kg/h - assume 1:1 molar ratio

5 mol HCl per liter solution = 0.182 kg HCl per liter solution

Liters of 5M = 41.5 kg/h/ 0.182 kg HCl/L= 228 L/h *(1.216) = 277.361 L/h

Convert to Kg/h: 277.361 L/h *(0.97 kg/L) = 269.04 kg/h HCl/IPA solution

Tank Size Calculations

Height = 2*Diameter

Volume = pi*Height*(Diameter/2)^2

Volume = pi*2*Diameter*(Diameter/2)^2

Tank 1: Volume = Flow rate*Residence time*1.15 = 24.8 L/min*2 min*1.15 = 57 L

0.057 m^3 = pi*2*D_1*(D_1/2)^2

D_1 = 0.33 m H_1 = 2*0.33 = 0.66 m

Tank 2: Volume = 24.8 L/min*5 min*1.15 = 143 L

0.143 m^3 = pi*2*D_2*(D_2/2)^2

D_2 = 0.45 m H_2 = 2*0.45 = 0.90 m

Tank 3: Volume = 24.0 L/min*16 min*1.15 = 442 L

0.442 m^3 = pi*2*D_3*(D_3/2)^2

D_3 = 0.66 m H_3 = 2*0.44 = 1.2 m

Impeller/Baffle Size Calculations

Tank 1: Impeller Diameter = D_1/3 = 0.33/3 = 0.11 m

Impeller height from base = H_1/3 = 0.66/3 = 0.22 m

Baffle length = D_1/10 = 0.33/10 = 0.033 m

Baffle width = D_1/20 = 0.33/20 = 0.0165 m

Baffle Dimensions: 4x 0.66x0.033x0.0165 m

Tank 2: Impeller Diameter = D_2/3 = 0.45/3 = 0.15 m

Impeller height from base = H_2/3 = 0.9/3 = 0.30 m

Baffle length = D_2/10 = 0.45/10 = 0.045 m

Baffle width = D_2/20 = 0.45/20 = 0.0225 m

Baffle Dimensions: 4x 0.90x0.045x0.0225 m

Tank 3: Impeller Diameter = D_3/3 = 0.66/3 = 0.22 m

Impeller height from base = H_3/3 = 0.1.3/3 = 0.44 m

Baffle length = D_3/10 = 0.66/10 = 0.066 m

Baffle width = D_3/20 = 0.66/20 = 0.033 m

Baffle Dimensions: 4x 1.3x0.066x0.033 m

Pumps and Blowers

P-101

Pressure Differential

P= ((1-1)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar = 100000 Pa

Volumetric Flow Rate

V=356.9 kg/h * 1/3600 h/s *1/790.6 kg/m^3 = 0.00013 m^3/s

Watts:

W = 100000 Pa*0.00013 m^3/s/(0.7*0.9)* 1/1000 = 0.020 kW

P-102

Pressure Differential

P= ((1-1)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar = 100000 Pa

Volumetric Flow Rate

V=205.07 kg/h * 1/3600 h/s *1/792 kg/m^3 = 0.000072 m^3/s

Watts:

W = 100000 Pa*0.000072 m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.017 kW

P-103

Pressure Differential

P= ((1-1)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar = 100000 Pa

Volumetric Flow Rate

V=800 kg/h * 1/3600 h/s *1/1000 kg/m^3= 0.00022 m^3/s

Watts:

W = 100000 Pa*0.00022m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.035 kW

P-104

Pressure Differential

P= ((1-1)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar = 100000 Pa

Volumetric Flow Rate

V= 2507.89 kg/h * 1/3600 h/s *1/1000 kg/m^3 = 0.00070 m^3/s

Watts:

W = 100000 Pa*0.00070m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.11 kW

P-201

Pressure Differential

P= ((15-1)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar = 1550000 Pa

Volumetric Flow Rate

V= 463.6 kg/h * 1/3600 h/s *1/794.72 kg/m^3 = 0.00016 m^3/s

Watts:

W = 1550000 Pa*0.00016m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.4 kW

P-202

Pressure Differential

P= ((1-1)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar = 100000 Pa

Volumetric Flow Rate

V= 221.79 kg/h * 1/3600 h/s *1/1149 kg/m^3 = 0.000054 m^3/s

Watts:

W = 100000 Pa*0.000054 m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.0085 kW

P-301

Pressure Differential

P=| (1-17.2369)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar| = 1573027.5 Pa

Volumetric Flow Rate

V= 143.48 L/h * 1/3600 h/s *(1 m^3/1000 L) = 0.000040 m^3/s

Watts:

W =1573027.5 Pa*0.000040 m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.10 kW

P-302

Pressure Differential

P=| (1-17.2369)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar| = 1573027.5 Pa

Volumetric Flow Rate

V= 179.9 L/h * 1/3600 h/s *(1 m^3/1000 L) = 0.000050 m^3/s

Watts:

W = 1573027.5Pa*0.000050 m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.12 kW

P-303

Pressure Differential

P=| (17.2369-17.2369)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar| = 50662.5 Pa

Volumetric Flow Rate

V= 202.32 L/h * 1/3600 h/s *(1 m^3/1000 L) = 0.000056 m^3/s

Watts:

W = 50662.5Pa*0.000056 m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.0045 kW

P-304

Pressure Differential

P=| (1-17.2369)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar| = 1573027.5 Pa

Volumetric Flow Rate

V= 809.282 L/h* 1/3600 h/s *(1 m^3/1000 L) = 0.000225 m^3/s

Watts:

W = 1573027.5Pa*0.000225 m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.54 kW

P-401

Pressure Differential

P= ((1-1)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar = 100000 Pa

Volumetric Flow Rate

V= 1227.79 kg/h * 1/3600 h/s *1/1113.954 kg/m^3 * = 0.000306 m^3/s

Watts:

W = 100000 Pa*0.000306 m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.049 kW

P-402

Pressure Differential

P= ((1-1)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar = 100000 Pa

Volumetric Flow Rate

V= 534.94 kg/h * 1/3600 h/s *1/661 kg/m^3 * = 0.00022 m^3/s

Watts:

W = 100000 Pa*0.00022 m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.03568 kW

P-403

Pressure Differential

P=((1-6)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar = 600000 Pa

Volumetric Flow Rate

V= 824.77 kg/h * 1/3600 h/s *1/784.5 kg/m^3 * = 0.00029 m^3/s

Watts:

W = 600000 Pa*0.00029 m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.278 kW

P-404

<u>Pressure Differential</u>

P=((6-1)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar = 600000 Pa

<u>Volumetric Flow Rate</u>

V= 269.04 kg/h * 1/3600 h/s *1/829.45 kg/m^3 * = 0.00009 m^3/s

<u>Watts:</u>

W = 600000 Pa*0.00009 m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.086 kW

P-405

<u>Pressure Differential</u>

P=((1-1)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar = 600000 Pa

<u>Volumetric Flow Rate</u>

V= 264.24 kg/h * 1/3600 h/s *1/661 kg/m^3 * = 0.00011m^3/s

<u>Watts:</u>

W = 600000 Pa*0.00011 m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.018 kW

P-406

<u>Pressure Differential</u>

P= ((1-1)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar = 100000 Pa

<u>Volumetric Flow Rate</u>

V= 1248.1 kg/h * 1/3600 h/s *1/1113.954 kg/m^3 * = 0.00049 m^3/s

<u>Watts:</u>

W = 100000 Pa*0.0004m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.077 kW

P-408

<u>Pressure Differential</u>

P= ((6-1)bar + 0.5 bar + 0 bar + 0.5 bar)*100000 Pa/bar = 600000 Pa

<u>Volumetric Flow Rate</u>

V= 900 kg/h * 1/3600 h/s *1/661 kg/m^3 * = 0.00039 m^3/s

<u>Watts:</u>

W = 600000 Pa*0.00039 m^3/s/(0.7*0.9)* 1/1000 kW/W = 0.36 kW

B-101[30]

<u>Fan Power:</u>

Airflow (ft^3/min) * Static Pressure (inch H2O) / (6356 * efficiency)

2938.7 kg/hr * 1 hr/60 min * 1 m^3/1.204 kg * 35.3147 ft^3/m^3 = 1435.3 ft^3 /min

(1435.3 ft^3 /min * 406.08 inch H2O (1 atm))/ (6356 * 0.7) = 130.98 hp
130.98 hp * 1 kw/1.36hp = 96.34 kW

Storage Tanks

Tank Volume = liquid volume* 1.15
Tank Radius = [(tank Volume)/(4*pi)]^(⅓)
Tank Height= Tank Radius* 4 - Assume a 2:1 Diameter to height ratio

Utility Cost

Impellers:
R-101: 29.31 watts * (1 kw/1000 watts) * (2 hours/batch) = 0.05862 kwh
R-202: 28.898 watts * (1 kw/1000 watts) * (2 hours/batch) = 0.0578 kwh
R-301: 13 watts * (1 kw/1000 watts) * (1.2 hours/batch) = 0.0156kwh
M-301: 593.6 watts * (1 kw/1000 watts) * (0.0833 hours/batch) = 0.0493 kwh
Total = 0.05862 + 0.0578 + 0.0156 + 0.0493 = 0.181 kwh
.181 kwh * (.0848 USD/kwh) = 0.0099 USD/batch * 1833 batch/per year = 28.13

Condensers:
E-101: 65.3 kw = 65300 W * (16.44 min * 60s/1min) (1 GJ/1 $\times 10^9$ J) = 0.0644 GJ
E-301: 169 kW = 169000 W * (5 min * 60s/1min) (1 GJ/1 $\times 10^9$ J) = 0.0507 GJ
E-401: 1 kW = 1000 W * (10.64 min * 60s/1min) (1 GJ/1 $\times 10^9$ J) = 0.0006385 GJ
Total: 0.0006385 + 0.0644 + 0.0507 = 0.116 GJ/batch
Cost: 0.116 * 18.72 USD/GJ = $2.17 USD/batch * 1833/batch = 3977.61 per year

Cooling water cost:
Table 8.3: .378 $/GJ
61.6566 kj/s* (1 GJ/s/1 $\times 10^6$ kJ/s) = 0.00006165 GJ/s
0.00006165 GJ/s * (.378 $/GJ) = 0.0000233 $/s
0.0000233 $/s*(3600s) * (24 hour) * (313 days) = $630.11 USD per year

Chilled Water Cost:
93.91 kj/s* (1 GJ/s/1 $\times 10^6$ kJ/s) = 0.00009391 GJ/s
0.00009391 GJ/s * (4.77 $/GJ) = 0.0004479 $/s
0.0004479 $/s * (3600s) * (24 hour) * (313 days) = $12,112.65 USD per year

Steam:
36kw + 145 kw + 33.9kw + 78kw + 52.1 kw + 98kw +38.94 kw = 481.94 kw = 481.94 kJ/s
(481.94 kJ/s) * (1 GJ/s/1 $\times 10^6$ kJ/s) = 0.00048194 GJ/s
(0.00048194 GJ/s) * (2.03 USD/GJ) = 0.000899 USD/s. (Turton, 2018)

(0.000899 USD/s) * (3600s) (24 hours) (313 days) = $26,457.68 USD per year.

Waste Treatment Cost

Block 1 (Dirty Water)
Flow is 2616.9 kg/h, which is about 2.617 ton/h, classified as non hazardous, disposed at $200 per ton[27]. The resulting cost is 2.617 ton/h × $200 = $523.40 per hour.

Block 1's hydrogen stream, flowing at 7.16 kg/h, undergoes pressure swing adsorption at a cost of less than $0.10 per kilogram when purifying hydrogen from a reforming reactor's output[27]. Applying this rate to 7.16 kg/h yields a cost of approximately 7.16 kg/h × $0.10/kg = $0.72 per hour.

Block 2 (Acid–Water Mix)
Flow is 443.577 kg/h, or 0.444 ton/h, classified as hazardous (strongly acidic), disposed at $2000 per ton. The resulting cost is 0.444 ton/h × $2000 = $888 per hour.

Block 4 (Decanter Aqueous Waste)
Flow is 937.96 kg/h, or 0.938 ton/h, classified as non hazardous (pH 7). Disposal occurs at $200 per ton, leading to 0.938 ton/h × $200 = $187.60 per hour.

Block 4 (Filter Waste)
Flow is 1367.48 kg/h, or 1.367 ton/h, classified as hazardous (flammables + acid). Using $2000 per ton, the cost is 1.367 ton/h × $2000 = $2734 per hour.

Batch Disposal Costs
Block 1 dirty water: $523.40/h. Block 2 acid–water: $888/h. Block 4 decanter: $187.60/h. Block 4 filter: $2734/h. The combined total is $523.40 + $888 + $187.60 + $2734 = $4333 per hour.

$4333 (per hour) * 24 Hr = 103392 * 313 days= 32549496 almost 32 million annually.

Material Balance

Table 32. Block 1 Material Balance

Name	**Meth Feed (33%)**	**SF-101 (Benzo feed)**	**SF-102 (NaBH4 feed)**	**H2 vent**	**Dryer 1 feed (wet solid)**	**N2 Feed**	**Meth recycle**	**Vapor N2 (post Meth sep.)**	**Cond. Meth (perfect sep.)**	**dryer 1 output solid**	**DM water feed - 3 washes**	**filter waste (all washes**	**wash out (wet solid)**	**dryer II air flow**	**dryer II air Vent**	**Dryer product (benzhydrol)**
Temp C	27	27	27	27	27	100	94.5	27	27	68	60	50	50	120	103	83
Pressure (bar)	1	1	1	1	1	1	1	15	15	1	1	1	1	1	1	1
Mass (kg)	356.9	225.0	44.8	7.16	619.5	2400.45	2584.85	2400.45	184.4	435.16	800	2526.07	327.3	3000	3109.1`	218.2
Liquid volume (L)	451.4	204.9	156.4	80468	620	4211320	3590.1	4211320	233	-	800	2472	-	-	-	-
Phase(s) of stream	l	s	s	g	70 (s) :30 (l)	g	g	g	l	s	l	(10) s:l (90)	(67) s:l (33)	v	v	s
Mass Compositions (kg)																
N2	0	0	0	0	0	2400.45	2400.45	2400.45	0	0	0	0	0	0	0	0
Benzophenone ($C_{13}H_{10}O$)	0	225	0	0	9.2	0	0	0	0	9.2	0	9.2	0	0	0	0
Sodium Borohydride ($NaBH_4$)	0	0	44.8	0	0	0	0	0	0	0	0	0	0	0	0	0
Methanol (CH_3OH)	356.9	0	0	0	205.1	0	184.4	0	184.4	20.7	0	20.7	0	0	0	0
Hydrogen gas (H2)	0	0	0	7.2	0	0	0	0	0	0	0	0	0	0	0	0
DM water	0	0	0	0	0	0	0	0	0	0	800	2290.91	109.1	0	109.09	0
Benzhydrol ($C_{13}H_{12}O$)	0	0	0	0	218.2	0	0	0	0	218.2	0	0	218.2	0	0	218.2
air	0	0	0	0	0	0	0	0	0	0	0	0	0	3000	3000	0
NaB(OCH3)4	0	0	0	0	187.0	0	0	0	0	187.0	0	187.0	0	0	0	0

Table 33. Block 2 Material Balance

Name	**37% aq HCl feed**	**Benzhydrol feed**	**R2 output**	**waste from decanter/ Water**	**Chloro product**
Temp C	83	83	83	25	25
Pressure (bar)	15	1	15	1	1
Mass (kg)	463.6	200	663.6	443.58	220.0
Liquid volume (L)	583.35	183.39	612.16	386	193.00
Phase(s) of stream	aq (l)	s	l (organic) :l (aq)	aq (l)	(organic) l
Mass Compositions (kg)					
Benzhydrol ($C_{13}H_{12}O$)	0	200	0	0	0
HCl	171.5	0	132.0	132.0	0
Chloro Diphenylmethane ($C_{13}H_{11}Cl$)	0	0	220.0	0	220.0
Water (H_2O)	292.1	0	311.6	311.6	0

Table 34. Block 3 Material Balance

Name	**DMAE feed**	**Chloro feed**	**R3 Output**	**Aq. 3M NaOH feed**	**Mixer output**
Temp C	175	175	175	175	175
Pressure (bar)	17.24	17.24	17.24	17.24	1
Mass (kg)	101.46	220.02	321.5	917.6	1227.79
Liquid volume (L)	143.48	179.9	202.32	809.28	1150
Phase(s) of stream	l	l	l	l	l (org) :l (aq)
Mass Compositions (kg)					
Chloro Diphenylmethane ($C_{13}H_{11}Cl$)	0	220.0	0	0	0
Dimethylaminoethanol (DMAE)	101.5	0	4.7	0	4.7
NaOH	0	0	0	97	53.7
Diphenhydramine HCl	0	0	308.9	0	0
Free Diphenhydramine	0	0	0	0	277.2
Neutral Byproducts	0	0	7.9	0	7.9
H2O	0	0	0	820.8	820.8
NaCl	0	0	0	0	63.5

Table 35. Block 4 Material Balance I

Name	**Crude DPH feed**	**Hexane feed**	**Decanter organic**	**decanter aqueous waste**	**5M HCl/IPA feed**	**Cryst. feed**	**Cryst. output**	**Hexane feed 2**	**Filter II waste (both washes)**	**Filter output (recycle feed)**
Temp C	25	25	25	25	25	25	5	25	25	25
Pressure (bar)	1	1	1	1	1	6	6	1	1	1
Mass (kg)	1227.79	534.94	824.77	937.96	269.04	1093.81	1093.81	264.24	1248.1	374.20
Liquid volume (L)	1150	809.28	1959.28	854	277.36	1440.74	1407.17	400	1795	-
Phase(s) of stream	l (org) :l (aq)	l	organic (l)	aq (l)	l	(20) s:l (80)	(30) s:l (70)	l	l	(67) s:l (33)
Mass Compositions (kg)										
Freebase Diphenhydramine	277.2	0	277.2	0	0	277.2	27.7	0	27.7	0
Hexane	0	534.9	534.9	0	0	534.9	534.9	264.2	938.8	124.7
Neutral Byproducts	7.94	0	7.9	0	0	7.9	7.9	0	7.9	0
H2O	820.8	0	0	820.8	0	0	0	0	0	0
HCl	0	0	0	0	41.5	41.5	41.5	0	41.5	0
Isopropanol	0	0	0	0	227.5	227.5	227.5	0	227.5	0
NaOH	53.7	0	0	53.7	0	0	0	0	0	0
Dimethylaminoethanol (DMAE)	4.7	0	4.7	0	0	4.7	4.7	0	4.7	0
Purified Diphenhydramine HCl	0	0	0	0	0	0	249.5	0	0	249.5
N2	0	0	0	0	0	0	0	0	0	0
NaCl	63.5	0	0	63.5	0	0	0	0	0	0

Table 36. Block 4 Material Balance II

Name	**Hexane feed for recycled product**	**Crystallizer feed (2nd pass)**	**crystallizer output (second pass)**	**Hexane filter wash Feed (one wash) (2nd pass)**	**Filter II waste**	**Filter output (wet) ->goes into dryer**	**dryer air flow (n2)**	**Dryer output (Final Pure DPH)**	**N2 and Hexane dryer output**	**Condensed hexane**	**Vapor n2 (perfect separation**
Temp C	25	25	5	25	25	25	100	70	87.6	27	27
Pressure (bar)	1	6	6	1	1	1	1	1	1	15	15
Mass flow (kg)	900	1274.2	1274.2	132.12	1034.42	371.86	2000	249.46	2122	122.4	2000
Liquid volume (L)	1362.4	1366	1801	200	1 565.88	-	3508772	255	-	-	-
Phase(s) of stream	l	s:l	s:l	l	l	s:l	g	s	g	l	g
Mass Compositions (kg)											
Free-base Diphenhydramine	0	0	0	0	0	0	0	0	0	0	0
Hexane	900	1024.7	1024.7	132.12	1034.42	122.4	0	0	122.4	122.4	0
Neutral Byproducts	0	0	0	0	0	0	0	0	0	0	0
H2O	0	0	0	0	0	0	0	0	0	0	0
HCl	0	0	0	0	0	0	0	0	0	0	0
Isopropanol	0	0	0	0	0	0	0	0	0	0	0
NaOH	0	0	0	0	0	0	0	0	0	0	0
Dimethylaminoethanol (DMAE)	0	0	0	0	0	0	0	0	0	0	0
Purified Diphenhydramine HCl	0	249.5	249.5	0	0	249.5	0	249.5	0	0	0
N2	0	0	0	0	0	0	2000	0	2000	0	2000
NaCl	0	0	0	0	0	0	0	0	0	0	0