Batch Versus Continuous Acetaminophen Production

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Letter of Transmittal

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Dear Dr. Etchells, Dr. Marchut, Dr. Stebe, Professor Vrana and Dr. Sieder,

The following report examines the production of acetaminophen via a batch and continuous process to compare process efficiency and economy. The plants will manufacture 30,000 Metric Tons of Type I acetaminophen powder to be sold at $4 a kilogram.

The continuous process was found to be five times more profitable than the batch process with an NPV of $37,800,000 USD and IRR of 33% compared to $7,300,000 USD and IRR of 18%. We recommend continued development of a continuous process as the impact on society, pharmacy and the environment could be profound.

We thank the department, the consultants and yourselves for the continued support, guidance and enthusiasm that has led to the successful completion of this project. We cherish the opportunity and experience.

Sincerely,

Sean Riksen Nathan Chau Shawn Byabato

Batch Vs. Continuous Acetaminophen Production

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Section 1: Abstract

Globally, acetaminophen is one of the most highly consumed over-the-counter drugs with an estimated market size nearing $10 billion at the close of 2021[1] . Price increases of over-the-counter drugs are driving the market towards generics which places significant pressure on the manufacturing segment to meet the new consumer demand. The largest manufacturers currently operate with an industry standard batch process to synthesize acetaminophen powder at a yield of 30,000MT/year [2]. The chemical engineering community proposes that a continuous process can offer significant benefits including reduced capital and operating costs, improved reaction control, and increased energy efficiency. This project demonstrates that at a production capacity of 30,000MT/year, under identical thermodynamic conditions, a continuous process is over 5 times more profitable than the corresponding batch process. At a price of $4/kg, the continuous process will yield a 15-year Net Present Value (NPV) of $38,000,000 with an Internal Rate of Return (IRR) of 33% compared to $7,300,000 and 18% for the batch process. The continuous process provides increasingly better financial returns as sale price increases relative to the batch process. Multiple factors contribute to the continuous process being more economical. The most significant factor is the lower equipment cost of $40,0200,000 USD for the continuous process compared to $67,300,000 USD for the batch process. Additionally, the continuous process sees lower operating costs in terms of both decreased energy consumption and lower operator costs. These conclusions provide justification for the continued development of a continuous process as the impact on society, pharmacy and the environment could be profound.

Section 2: Introduction

2.1: Project Background

The pharmaceutical market, one of the largest industries in the world, continues to grow rapidly owing to increasing consumer health awareness, improved distribution channels, urbanizing lower-middle income nations and the lasting effects of the pandemic[3],[4]. The upstream sector is primarily focused on the formulation of Active Pharmaceutical Ingredients (APIs), the drug components that produce the desired biological effect. These products are then distributed by product segment[5]. Analgesics are a class of drugs within the pharmaceutical market that have seen the most significant increase in demand over the last 3 years[6]. These drugs relieve pain and reduce inflammation with both prescription and over-the-counter products available[7]. This project addressed manufacturing the API acetaminophen, one of the most consumed over-the-counter drugs on the market. Acetaminophen has an anti-inflammatory effect and is thus prescribed for a wide variety of chronic diseases and a myriad of clinical issues, explaining its strong demand. Acetaminophen is manufactured in powder form. This powder is then converted to tablets, capsules, fluid solutions or IV fluids. The acetaminophen portion of the bulk analgesics composes around 80,000 metric tons a year amounting to an approximated value of $400 Million. This estimation considers the market availability price-range between $3.5 to $5 globally[2].

Acetaminophen is a small molecule produced by a non-biological / synthetic process. The current batch process consists of starting with phenol, a commodity chemical, which is reacted to form nitro-phenol. There are two isomers of nitro-phenol which must be separated by distillation. Then the para isomer is then converted into amino phenol by hydrogenation. All are liquid phase reactions. The nitration requires two liquid phases, and the hydrogenation is a gas-liquid reaction with a solid catalyst. In the last step of this process, acetic anhydride is added, which precipitates the final product. This crystal product is then recrystallized for purity and converted into tablets with the addition of excipients which enhance digestibility[8]. The solids handling steps to produce the tablets are outside of the scope of this project. This project culminates with the formation of purified and dried acetaminophen crystals.

Manufacturing cost is a critical factor for success because consumer behavior is strongly dictated by price. Chinese and Indian entrances into acetaminophen production continue to drive global prices down. For example, in 2002, the US list price for acetaminophen was over $8 and as mentioned above, this price has practically halved in 2022. It is important to recognize however that the extreme demand experienced over COVID has presented some variability in the price that is likely to have lagging effects over the short to medium term. The production process is historically and presently performed as a batch process as opposed to a continuous process. This reliance on batch processes can be attributed to multiple factors, including batch control, simpler reaction pathway steps, lack of adequate scaled continuous reactors and varying performance of continuous crystallizers. However, continuous manufacturing is thought to present a multitude of potential benefits in terms of time and resource savings, flexibility, and control over reaction conditions including concentration, pressure, and temperature[9]. It is proposed that a continuous process could be cheaper and more sustainable. The aim of this project is to compare the manufacture of acetaminophen by batch and continuous processes to determine whether and under what conditions the purported benefits can be achieved.

2.2: Project Goals

Acetaminophen is a widely produced drug typically manufactured in batch processes. It has been suggested that profits might be enhanced, and production costs might be reduced by changing to a continuous process. In this report, batch and continuous manufacturing process trains will be designed to conduct a thorough cost comparison and to gain an understanding of methodology to keep capital costs of the equipment and operating costs of the facility to a minimum.

There are several routes for acetaminophen synthesis. It was recommended to focus on a process that begins with p-nitro phenol, which undergoes hydrogenation to p-amino phenol, to which acetic anhydride is added to yield the API. However, the solvent for the early steps is often benzene and thus an analysis of reaction pathways to limit harmful solvents and byproducts as well as to minimize cost will be conducted. It is also suggested by the project consultants that purchasing necessary reactants may be more economical than synthesizing them; again, a comparison will be completed to make an educated decision in this vein regarding for p-aminophenol and acetic anhydride.

The batch and continuous processes will be designed under identical thermodynamic conditions and will follow the same order of operations with the goal of allowing a 1:1 comparison. A complete optimization that will incorporate capital costs, operating costs, and profits will be conducted following the process train design to build into a sensitivity analysis that will form the basis for comparison.

2.3: Production Goals

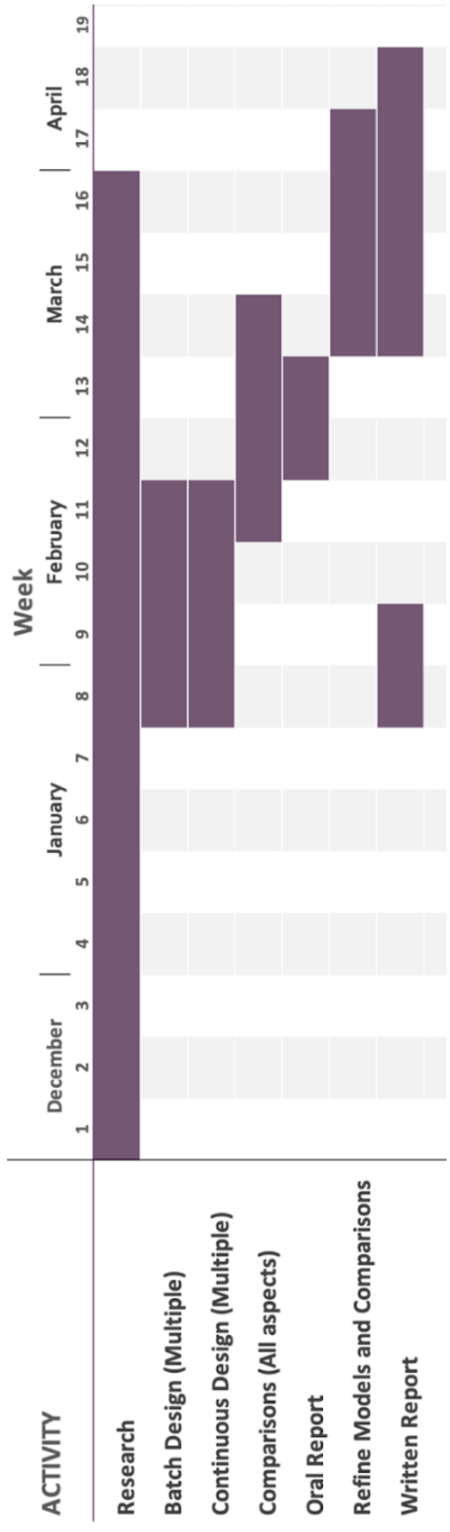
The batch and continuous plants are designed to produce 30,000 metric tons per year of dry powder acetaminophen. The batch process will operate for 24 hours across 292 days (20% down time), producing 102.74 metric tons a day. The continuous process will operate for 328.5 days (10% down time) producing 91.32 metric tons a day, requiring a throughput 63.42 kg/min.

2.4: Design Process & Deliverables

This project assignment had no limitation with respect to plant location or synthetic process. Thus, the plant location and synthetic process were selected after consideration of several factors, including labor cost, supply availability, utility reliability and market trends alongside operator safety and waste management. An initial exploration of available patents allowed selection of a synthetic pathway. Unit operations were then examined for both batch and continuous processes and the process flow diagram for each process was created in parallel. The completion of fundamental kinetic and thermodynamic analyses allowed for concurrent assessment of reactor sizing, with guidance from industry norms, in order to define time scales and throughput. As this assessment developed, the capital investment correlations were established to help define unit sizing to be most economical. The results of the sizing provided capital expenditure, operating expenditure, and profitability.

The final design compares a batch and a continuous process, ultimately making a recommendation as to which is a wiser investment.

2.6: Project Time Chart



Section 3: Innovation Map

The Innovation Map section has been removed from the process design report

Section 4: Customer Requirements & Critical-To-Quality (CTQ) Variables

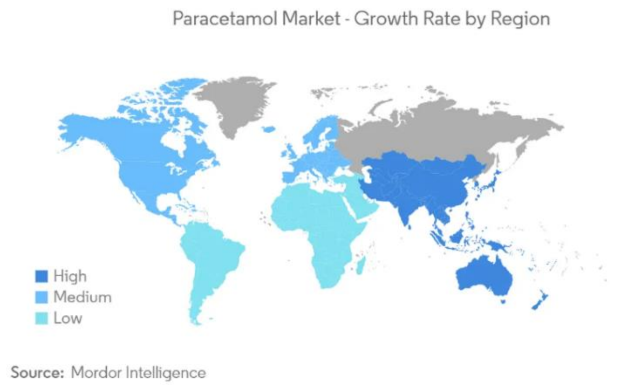
Customer Requirement	Technical Requirement Critical to Quality (CTQ)	Typical Values
Pure powder product	Uniformly Type 1 crystal	>99.9% Type 1 polymorph
	Uniform Crystal Size Distribution	<150 µm particle size spread
	Low Impurity level	>99.8% purity of powder
Dry product	Packaged powder is dry	<1% powder wetness
Pure Acetic Acid solution	Low Impurity level	>99.8% purity of solution 60% aqueous Acetic Acid

Section 5: Market and Competitive Analysis

In light of the extreme pandemic related public-health expenditure over the last two years, it is expected that many countries will restrict public health spending in the near future in an attempt to reduce sovereign indebtedness. This setting provides a significant opportunity for the private sector to support this trend by providing a competitive, capitalistic market within which health industries can flourish. One of the primary shifts in demand during this period has been the growing global need for medicines. For example, according to the Fitch Solutions *Global Pharmaceuticals and Healthcare Report* [10], the 1.2 trillion USD global pharmaceutical market is forecasted to grow at an unprecedented 6.3% CAGR over the next 5 years. Within this market, over the counter (OTC) drugs are experiencing the most significant growth in demand, specifically oral analgesics (painkillers), as numerous national healthcare authorities recommend their use for managing fevers and aches[11]. Acetaminophen (US) or paracetamol (EU/Asia), the Active Pharmaceutical Ingredient (API) in the commonly known private label brand Tylenol, is anticipated to have the most significant demand growth among competing analgesics. In addition, lower-priced private label analgesics are predicted to double the demand growth rate of any brand name product[6]. As such, a clear economic opportunity is present to revolutionize acetaminophen manufacturing to be a cheaper and greener process.

The global acetaminophen market value in 2021 closed at an estimated 9.44 billion USD and is expected to reach nearly 15 billion USD by 2030[1]. Rising chronic disease and pain-management conditions alongside the dissolution of many major opioid producers plays a vital role in accelerating market size. These market pressures are compounded by a significant increase in doctor prescriptions, general consumer awareness and the urbanizing of low to middle income nations[12]. It is important to recognize that generics are becoming increasingly popular and new generic retailers are flooding the market creating significant barriers to entry. A recent trend towards chemical sustainability also presents challenges for new entrants.

Sales through retail pharmacies account for 28.5% of total market share of which North America makes up 33% of sales, Europe and Asia combine to 45% and South Asia and Latin America combine for 20%[13]. The key players are represented by Abbott, Janssen Pharmaceuticals Inc (Johnson and Johnson), Bristol-Myers Squibb and Company, Proctor and Gamble Company and Mallinckrodt Pharmaceuticals among six other comparable competitors. Interestingly, manufacturing is dominated by India and China, composing an estimated 80% of total production. The dominance of the market by these countries may be attributed to the cost of labour and land as well as strategic distribution locations. The Asia-Pacific region is also dominating the new demand trends as the chronic disease burden surges in the ageing populations.



Finally, the B2B market is forecasted to be the most defensible new entrant segment as consumer purchase behaviors are increasingly disconnected from traditional retail with a desire for a faster experience with fewer interactions with sales reps. Buyers, also in the B2B spaces, are increasingly digital and this avenue presents the incumbent enterprise with an opportunity to vertically integrate. At the scale of this project, vertical integration could become a major price differentiator especially with the rising preference of generics.

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Section 6: Product Concepts & Superior Concept

This design project addresses the manufacture of acetaminophen powder at global scale in response to the price competition in the market. The powder is made available as a B2B product that will be distributed to plants for tablet, capsule etc. formulation.

6.1: Polymorph

Firstly, acetaminophen crystallization presents numerous challenges as the small molecule is polymorphic with five variations. Three of these morphs are substantially more prevalent at the relevant pressures and temperatures, but Form 1 and Form II are the only morphs that occur under the operating conditions of this plant. Form I crystals are monoclinic and the most thermodynamically stable form of acetaminophen at room temperature. Form II crystals are orthorhombic metastable at room temperature and will spontaneously convert to Form I when exposed to increasing temperatures. While Form I is the more stable form, these crystals display poor compressibility due to the absence of slip planes in the crystal structure. This compressibility is necessary when the crystal undergoes plastic deformation during compression; to overcome this deficiency, excipients are added which increases both the time and cost of manufacturing. As such, a strong case has emerged to operate in conditions that favor Form II as this crystal structure already comprises of well-defined slip planes. However, consistent Form II growth has not been achieved on a bulk/scale to elute a purity higher than 50% whereas Form I can obtain purities >99%. [14] Thus, this project will build on established processes of obtaining high purity Form I crystals.

6.2: Acetic Acid

Acetic acid is a byproduct of the prominent reaction as water hydrogenates the excess acetic anhydride in solution. Some of this acetic acid is recycled for recrystallisation purposes, however, most will be sold. Acetic acid is an organic compound used in many chemical manufacturing plants, in food additives and in petroleum production[15]. This plant can thus make significant revenue for the sale of this component. It was found that the price of acetic acid varies depending on percentage of acetic acid in solution. Naturally, the higher percentage the larger the sale premium. This project will thus isolate the highest purity acetic acid possible while maintaining cost efficiency. It was found that the process elutes 63% acetic acid in water solution following flash distillation. To obtain higher purity, complex distillation would be required. This further treatment was rejected as an option, as the project focus is to compare overall profitability between the batch and continuous processes for the production of acetaminophen. As both processes could isolate the same compositions, no further optimization was performed.

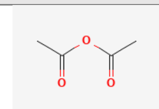
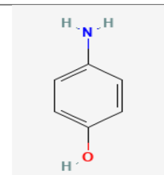
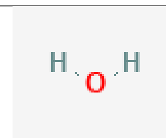
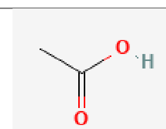
Section 7: Competitive (Patent) Analysis

This analysis reveals a paucity of relevant information. The patents for major producers appear to be listed online, however access is not possible or process specification omitted from public access. It was observed that substantial new patent work on elaborate and new reaction pathways to produce acetaminophen were present. These pathways included numerous new starting materials that were potentially more sustainable and many of these were found in the European Patent Office. For example, application 09425226.9 criticized the non-quantitative nitration of phenol to para-nitrophenol as the ortho position was equal to as much of 66% and the byproducts presented difficult separability as well as strong pollutant qualities. The applicants thus presented new reactants just as neopentyl bromide or sodium phenoxide to allow for nitration with neopentyl phenyl that allowed the subsequent acetylation to be fast and quantitative[16]. This project evaluated a number of such patents; however, these new inventive methods had no scalable data available and often required elaborate unit operations. Further, many of the improvements were associated with the production of the p-aminophenol. Since this project builds the process trains based on the procurement of p-aminophenol, these improvements were not relevant to this project. Throughout this report, the assumption is made that p-aminophenol will be available to procure at the necessary quantities.

Finally, no available patent on a process with scale for either traditional or inventive processes. Thus, lab experiments and a process made available by project authors, facilitated much of the decision making regarding the process synthesis.

Section 8: Preliminary Process Synthesis

Table 8.1 Participating Chemicals [17, 18, 19, 20]

Chemical	Molecular Weight	Chemical Formula	Structure	Assumed Cost $/kg
Acetic Anhydride	102.09	$(CH_3CO)_2O$		1.5
P-Aminophenol	109.13	C_6H_7NO		2.5
Water	18.015	H_2O		0.00211
Acetic Acid	60.05	CH_3COOH		1

This report addressed the synthesis of acetaminophen assuming that p-aminophenol will be purchased as a reactant. It is important to recognize that the synthesis of p-aminophenol follows a catalytic reduction of nitrobenzene in the presence of zinc and ammonium chloride[21]. Ammonia chloride has significant environmental effects and is a serious eye hazard for operators[22]. The resultant phenylhydroxylamine requires recrystallisation to ensure purity and this step demands either benzene-light petroleum or benzene. Both chemicals are highly flammable, and benzene is a particularly hazardous chemical that can cause bone marrow deterioration, decrease ovary sizes and pregnancy issues as well as being a known carcinogen[23]. These reasons support the decision to procure p-aminophenol as opposed to manufacture the molecule. Based upon discussion with multiple distributors, an optimized combination of suppliers could satisfy the demand of this plant.

The price of this commodity was thus obtained from project consultant Mariella Juhasz at $2.50/kg.

According to lab processes obtained from the University of Pennsylvania Chemistry Department and corroborated by two other university programs [24,25], the first step in the synthesis is to acetylate p-aminophenol. This is done with acetic anhydride in excess and water to convert the excess acetic anhydride to acetic acid.

1. $(CH_3CO)_2O + C_6H_7NO \rightarrow C_8H_9NO_2 + CH_3COOH$
2. $(CH_3CO)_2O + H_2O \rightarrow CH_3COOH$

At laboratory scales, the reaction occurs within 5-15 minutes at a temperature range between 70-80°C. This project uses the upper limit of 80°C for crystallization yield purposes. To optimize the ratio of reactants, multiple coupled variables were evaluated that include solubility [A.3], cost [A.7], reactant excess [A.1, 10], and reactor size volume [11] and this optimization led to the most economical overall mass and energy balance and values are shown in Figure 8.1 and 8.2. The detailed description of choices is outlined in the sections referenced.

The solution is then cooled slowly to obtain crystals and slurry is filtered to isolate solids. The filter mother liquor is sent for a distilled separation as the acetic acid and water can be efficiently separated from any solids and impurities leading to reactant recycle streams as well as saleable aqueous acetic acid product. The crystals are then redissolved to be decolorized/purified with activated carbon or sodium dithionite. Considering both activated carbon and sodium dithionite composition require empirical data that was not available, this project uses activated carbon as suggested by[26] and conservative estimates were made on quantity required. This purified solution is then recrystallized and filtered before drying. Again, the filter mother liquor is distilled and recycled.

Figure 8.1 Flowsheet showing distribution of chemicals for batch acetaminophen synthesis

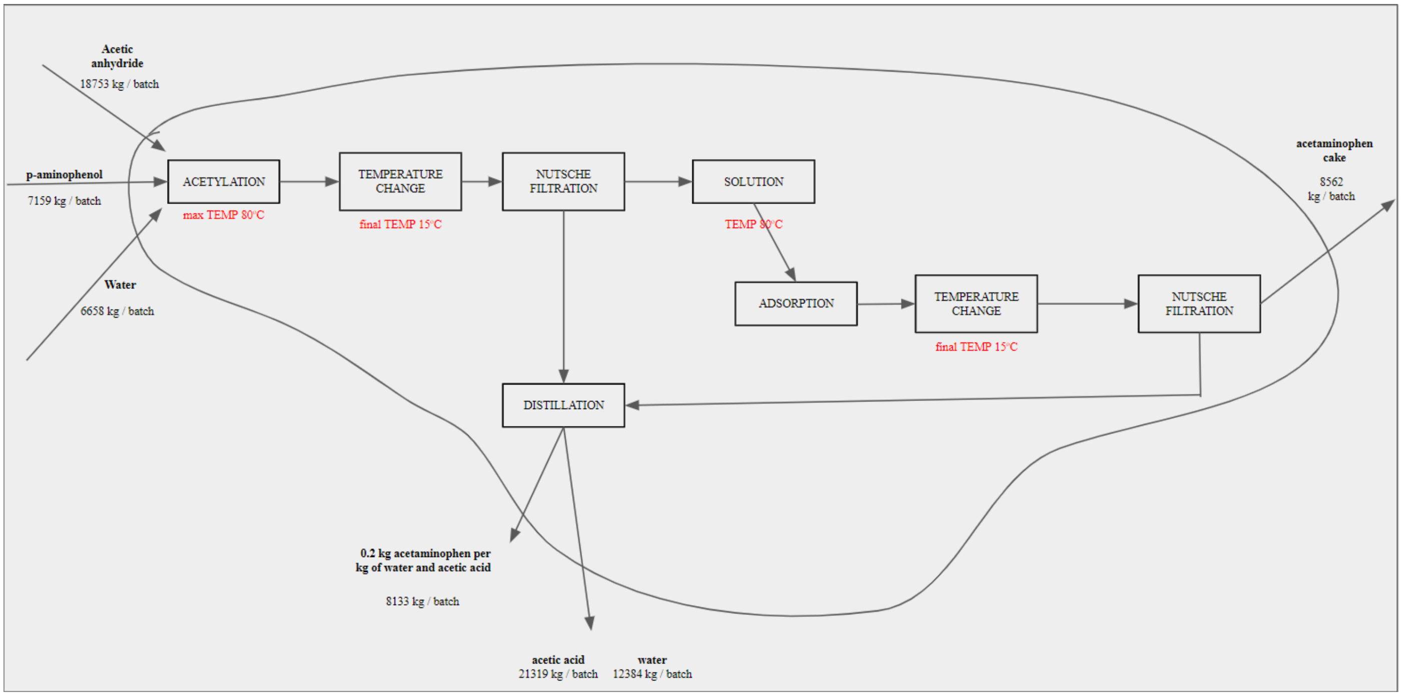
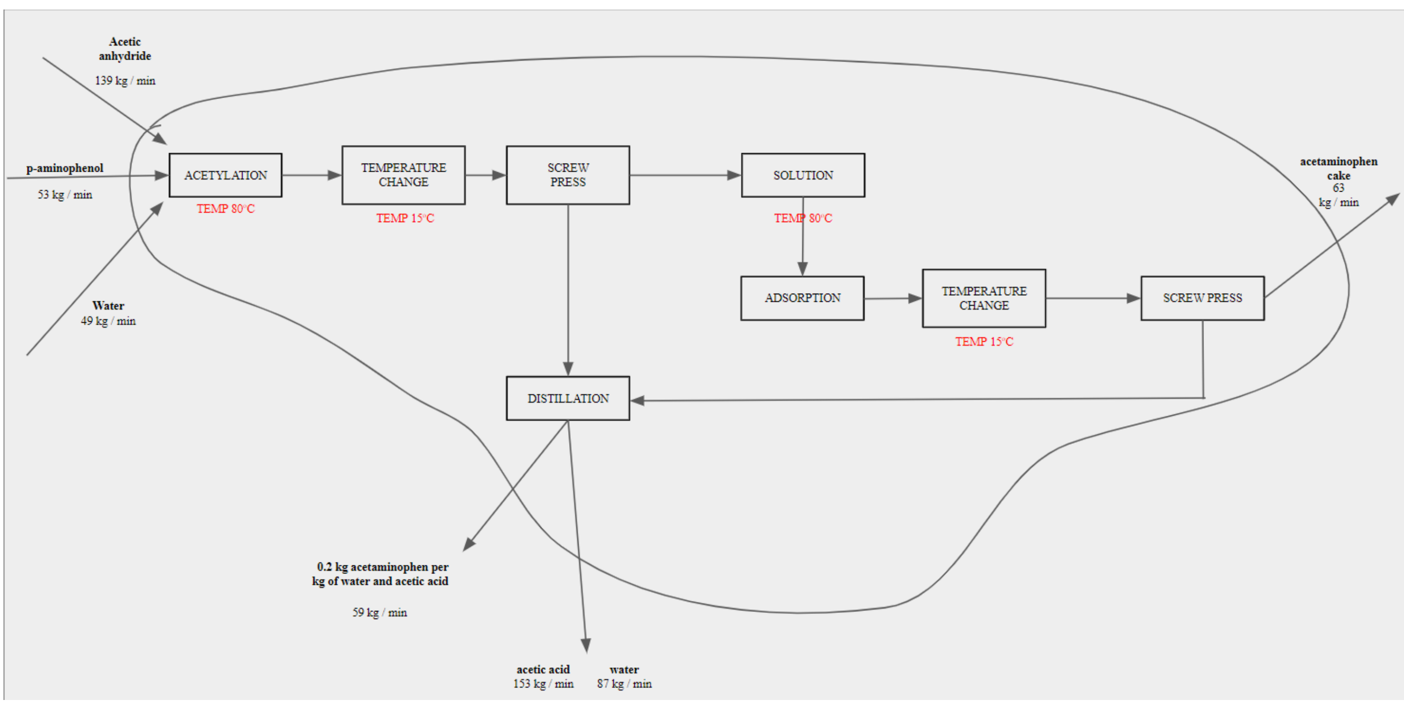


Figure 8.2 Flowsheet showing distribution of chemicals for batch acetaminophen synthesis



Section 9: Assembly of Database

9.1: Reactant/Product Properties

To perform calculations and to understand the behavior of the materials modeled, fundamental properties of all the reactants and products are provided. The relevant materials are acetaminophen, acetic acid, water, p-aminophenol, and acetic anhydride. The relevant properties are molecular weight, density, heat capacity, and heat of formation

Table 9.1 Fundamental Molecule Properties [27, 28, 29, 30]

Chemical	Molecular Weight	Density (kg/m^3)	Heat Capacity (J/mol.K)	Heat of Formation (kJ/mol)
Acetic Anhydride	102.09	1080	168.2	-625
P-Aminophenol	109.13	1130	191.4	-194.1
Water	18.015	1000	75.9	-286.3
Acetic Acid	60.05	1030	123.1	-484
Acetaminophen	151.16	1260	190	-297.3

In addition to those properties, the crystallization energy of acetaminophen is 27.6 kJ/ mol[31]

9.2: Component Prices

Table 9.2 Raw Material Prices [33]

Raw Material Required (kg/batch)	Source	Cost ($/kg)
Water	0.80 $/1000gal – Sieder book	0.000211
P-Aminophenol	1.2 alibaba & Mariella	1.20
Acetic Anhydride	from Mariella	1.50
Acetic Acid	from Mariella	1.00
Acetaminophen	from Mariella	3.00-5.00

9.3: Reaction Properties

Two reactions require characterization for this system: 1. p-aminophenol and acetic anhydride to form acetaminophen and acetic acid and 2. acetic anhydride and water to form acetic acid. As noted by Jiang et.al[34], reaction 1 can be modeled as an irreversible pseudo first order reaction when acetic anhydride is in substantial excess of p-aminophenol. According to Hirota et.al[35], reaction 2 follows three irreversible steps observed to represent first-order kinetics.

1. $(CH_3CO)_2O + C_6H_7NO \rightarrow C_8H_9NO_2 + CH_3COOH$
2. $(CH_3CO)_2O + H_2O \rightarrow CH_3COOH$

Both reactions must proceed within a reasonable timescale and to characterize the reaction rates, the Arrhenius equations are provided…

Arrhenius: $\mathrm{k} = Ae^{(-\mathrm{Ea}/\mathrm{RT})}$

Jiang et al[34] report the activation energy of reaction 1 to be 37310 J/mol. The report compared the reaction rate as a function of temperature and input the reaction rate, activation energy, gas constant, and temperature to determine the Arrhenius pre-exponential factor for the temperatures of 323 K and 343 K. This temperature range corresponds to the operating range of temperatures for this project. It is important to note that while one work suggested that the complex conditions for equalmolar conditions suggest 2nd order kinetics, the reaction kinetics from Jiang et.al are reasonable as the authors note the hydrolysis step is significantly faster than the rate limiting step. The authors also note that their work was corroborate by two other labs. As noted above, this reaction in this experiment will operate between 319 and 343 K and thus uses 11293 s^{-1}.

Table 9.3: Arrhenius Correlation Data

T (K)	k (1/min)	A (1/min)	A (1/s)
323	0.61	658990	10983
343	1.41	677576	11293

For the second first order reaction, Hirota et.al[35] observed and activation energy of 43000 J/mol and Arrhenius pre-exponential factor to be e^9 or 8103 s^{-1}. Before progressing with plant design, it was necessary to ensure reaction 1 proceeded faster than reaction 2 across the temperature range 273-373 K. Over the entire range, the first reaction was at least 8 times faster than the second endorsing the use of these reactions as essentially all possible product will be produced before the acetic anhydride is consumed. Further, the k_2 is reported at 0.351 at 353 K and using the integrated rate law ($[A]=[A]_0*e^{-kt}$), 99.9% conversion is achievable in 32 minutes, an acceptable reaction time.

Table 9.4: Kinetics as a function of temperature

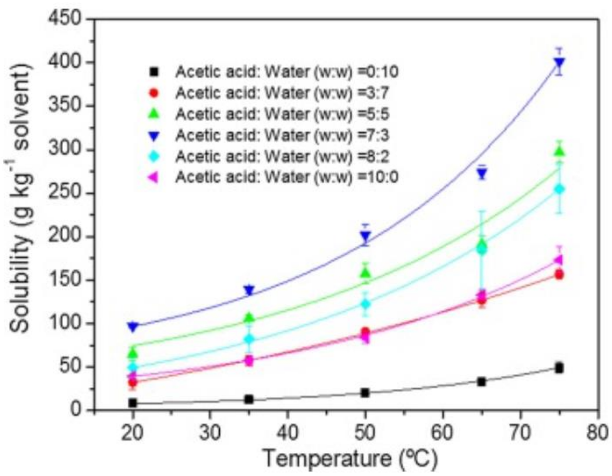
T (K)	k_1 (1/s)	k_2 (1/s)	k_1/k_2
273	0.00082	0.00005	17.1
293	0.00252	0.00017	14.4
313	0.00671	0.00054	12.4
333	0.01587	0.00146	10.9
353	0.03404	0.00351	9.7
373	0.06730	0.00771	8.7

Next, the heat of reaction was also calculated for the reactions to aid in determining the temperature change over time. The heat of formation for all the components were found; the heat of reaction was calculated by subtracting the product's heat of formation from the reactants. The first reaction is endothermic with a heat of formation of 37800 J/mol. The second reaction is exothermic with a heat of formation of -58900 J/mol.

9.4: Solubility Properties

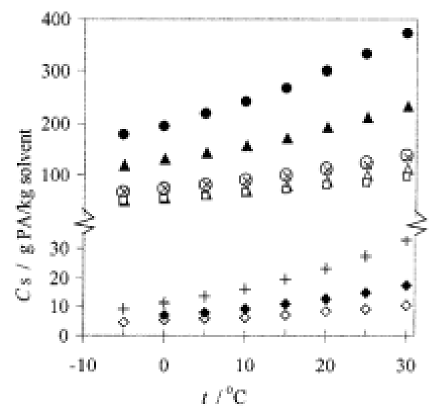
In a follow up study, Jiang et.al[36] display the solubility of acetaminophen in solvents of different water and acetic acid weight compositions. These solubility curves were corroborated by two other sources also demonstrated below[37,38].

Figure 9.1: Solubility by composition [36]



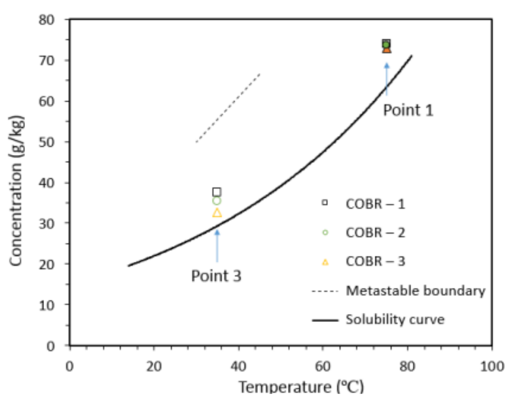
Solubility of paracetamol in different ratios of acetic acid to water

Figure 9.2: Solubility by solvent [37]



Solubility, Cs, of paracetamol versus temperature in, ●,methanol; ethanol; x, 1-propanol; o, 2-propanol; Δ acetone; □ butanol; + , acetonitrile; ♦water; ◊ethyl acetate

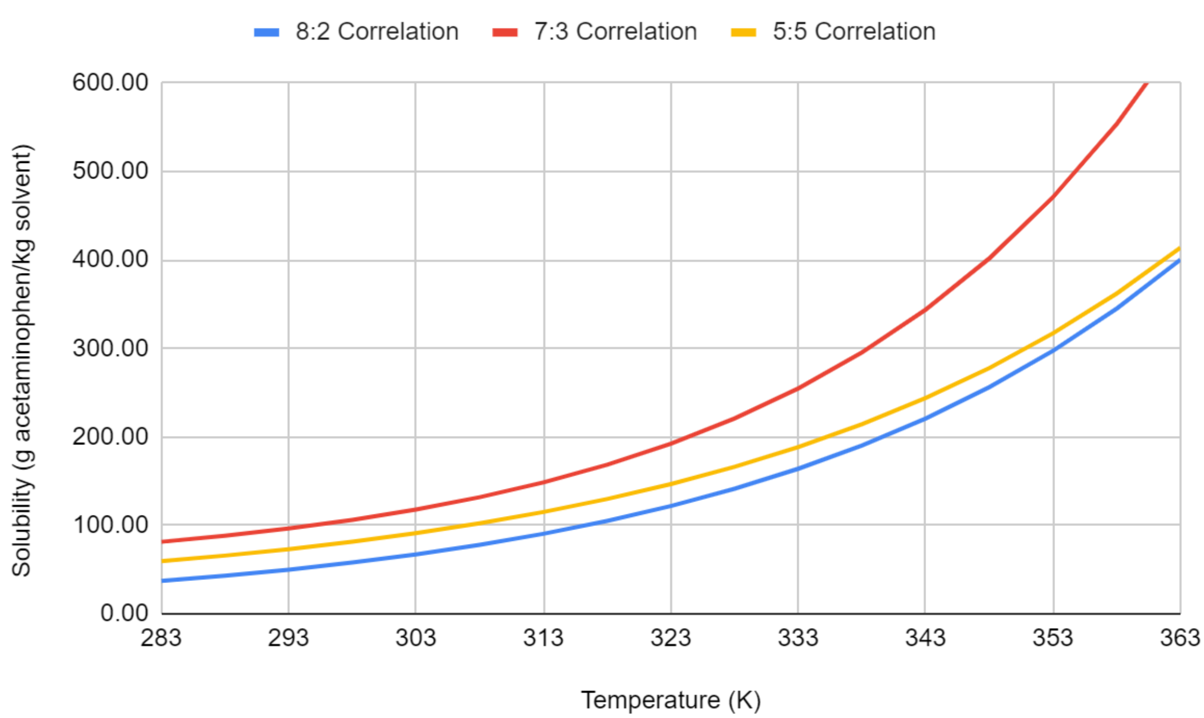
Figure 9.3: Solubility with Metastable Zone Width [38]



Data on metastable zones and supersaturation. Solubility, MSZW and crystallization measured gravimetrically in a solvent ration of Acid:H2O = 1:9

The first goal was to select the desirable water and acetic acid composition that awards the greatest solubility to satisfy the large production volume. The greater the solubility, the less the solvent needs which leads to smaller equipment sizes and this was assumed to lead to a reduction in costs. As the data from both Jiang et al and Kramer et.al places the acetic acid and water solvent in between ethanol and methanol solubility curves, no further optimization was performed for solvent composition., A solute composition of 7:3 weight ratio of acetic acid to water was decided upon and the data was uploaded to fit an exponential curve for succeeding iterative solutions [A3]. This is shown in Figure 9.4.

Figure 9.4: Solubility Data used for model



The solubility function in g acetaminophen/kg solvent becomes…

7:3 Composition: $0.001501 * e^{(0.0355626 * \text{TEMP})} + 46.06541$

To optimize cost, this identical analysis was performed on the 8:2 and 5:5 acetic acid: water ratios. The equations were found to be

8:2 Composition: $0.008161104 * e^{(0.029753937*\text{TEMP})}$

5:5 Composition: $0.01554 * e^{(0.027955*\text{TEMP})} + 17.01735$

With this equation, the amount of dissolved acetaminophen at any given temperature can be determined. More importantly, this also gives information on the amount of crystalized acetaminophen as the total amount minus the dissolved amount. The consultants advised that a solution composition greater than 300 g acetaminophen/kg solvent will prevent the slurry from stirring or flowing well. As such, recognizing the temperature swing from 80 ºC to 15 ºC, an optimization was performed to obtain the greatest solubility difference within this range. For the 7:3 acetic acid: water weight ratio, the solubility ranged from 88.18 to 471.02 g acetaminophen/kg solvent with an artificial cap at 300. As such 211.82 g acetaminophen can be extracted from 1 kg of solvent. The 8:2 solvent ratio ranged from 42.98 to 297.31, such that 254.33 g acetaminophen can be extracted from 1 kg of solvent and the 5:5 solvent ratio ranged from 65.77 to 317.02 such that 234.23 g acetaminophen can be extracted from 1 kg of solvent. To minimize solvent used and thus equipment size, the 8:2 acetic acid to water weight ratio solvent was ultimately selected.

9.5: Heating/Cooling Agent Properties

The heating and cooling agents considered are those that appear in SuperPro Designer…

Cooling agents: cooling water, chilled water, NaCl brine, $CaCl_2$ brine, glycol, and freon

Heating agents: hot water, 5 atm steam, and 35 atm steam as heating agents.

SuperPro Designer provides the price per metric ton for the agents. Furthermore, as an accuracy check, these prices were compared to the price estimates in the Seider textbook[32]. As the Seider textbook does not contain the same agents, three agents - chilled water, freon, and 5-atm steam - were assessed against the most closely related agent as Seider. There are some differences. For example, Seider prices steam at ~4.5 atm around 10% more than SuperPro Designer, although SuperPro Designer is expected to be more expensive considering the increased pressure. For the purposes of this report, the 10% difference is taken as acceptable deviance. SuperPro Designer prices chilled water to cost 3.8 times that of the Seider textbook; thus, using SuperPro Designers cost is conservative. Finally, freon was approximated with 10 ^{o}F refrigerant, and cost 24 times more in SuperPro Designer. With the differences addressed in the following section, the SuperPro Designer cost is taken to reflect expectation.

Table 9.5: Cost of Heat Transfer Agents

	SuperPro		Seider		Comparison
Agent	$/Unit	Cost ($/s)	$/Unit	Cost ($/s)	SuperPro/Seider
Chilled water	0.4 $/MT	0.00772	5 $/GJ	0.00203	3.798
Freon	0.15 $/MT	0.02228	6.47 $/GJ	0.00092	24.15
Steam (5 atm)	12 $/MT	0.00192	13.2 $/1000kg	0.00211	0.909

To minimize costs, the energy of cooling agent per dollar was calculated to provide a standardized point of comparison. Utilizing heat capacity, temperature change, and cost, the ratio of joules per dollar was calculated. Note, this number was to be maximized to minimize utility cost. Another consideration is the temperature of the cooling agent as this will influence the cooling rate, thus potentially allowing for smaller or fewer vessels. NaCl brine and $CaCl_2$ brine were the optimal solutions recognizing the temperature limit of cooling water and for the heating agents, all three can be optimal depending on the temperature.

Table 9.6: Heat Exchange Agents Demands

	T in	T out	Heat capacity	Energy/Mass	Cost/Mass	Energy/Cost	Cost ratios
Heating agents	K	K	J/gK	J/kg	$/MT	J/$	Normalized
Hot water	313	303	4.184	4.18E+04	0.05	8.37E+08	1.00
5 atm Steam	425	425	-	2.11E+06	12.00	1.76E+08	4.76
35 atm Steam	515	515	-	1.76E+06	20.00	8.78E+07	9.53

Table 9.7: Comparison of Agents Utility

	T in	T out	Heat capacity	Energy/Mass	Cost/Mass	Energy/Cost	Cost ratios
Cooling agents	K	K	J/gK	J/kg	$/MT	J/$	Normalized
Cooling water	298	303	4.184	-20920	0.05	-4.18E+08	1.00
NaCl Brine	263	273	3.45	-34500	0.25	-1.38E+08	3.03
$CaCl_2$ Brine	243	253	2.7	-27000	0.25	-1.08E+08	3.87
Glycol	263	273	2.281	-22810	0.35	-6.52E+07	6.42
Chilled water	278	283	4.184	-20920	0.40	-5.23E+07	8.00
Freon	269	270	0.96	-960	0.15	-6.40E+06	65.38

Note that assumptions were made for NaCl brine and $CaCl_2$ brine's heat capacity. SuperPro Designer does not state the percentage of salt which affects heat capacity. The freezing point must be below the initial temperature and thus a middling heat capacity was chosen. For example, with the NaCl brine, the brine must consist of 14-22% NaCl to have a freezing point below -10 ^oC[39] a middling 18% was estimated which has a heat capacity of 3.45 J/gK.

9.6: Overall heat transfer coefficient

The overall heat transfer coefficient for the jacketed vessel and heat exchangers were estimated using Thermopedia[40]. As heat exchangers will be more efficient than jacketed vessels, the same number will be used for heat exchangers as a conservative estimate.

Initially, due to the corrosive nature of heated acetic acid and concerns for sanitation in the final pharmaceutical product, glass lined steel was the proposed material for the vessels and heat exchangers. However, as some vessel sizes exceed 40 m^3 in both batch and continuous, Hastelloy was chosen due to its stable properties. As Hastelloy has a thermal conductivity of 12 W/mK[41], lower than both carbon steel, 43 W/mK[42], and stainless steel 14.3 W/mK[43], thus the overall heat transfer coefficient of glass lined steel was used as a more conservative estimate even though the Hastelloy thermal conductivity is decently higher than glass lined steel's 1.2 W/mK[44].

Industry consultants advised that the NaCl brine and $CaCl_2$ brine overall heat transfer coefficients would behave similarly to chilled water and thus the following combinations of cooling/heating agent and overall heat transfer coefficients were decided upon.

Table 9.8: Operating Conditions of Agents

	T in	T out	Cost/Mass	Cost ratios	Overall heat transfer coefficient
Heating agents	K	K	$/MT	Normalized	W/m^2K
Hot water	313	303	0.05	1.00	310
5 atm Steam	425	425	12.00	4.76	310
35 atm Steam	515	515	20.00	9.53	310

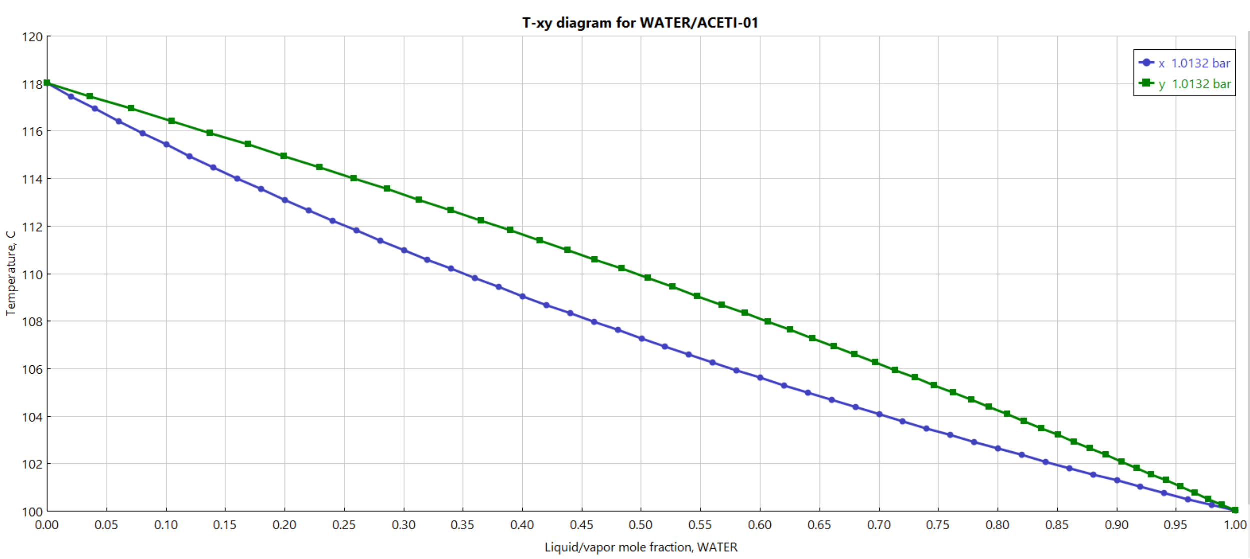
Table 9.9: Determination of Optimum Cost Performance

	T in	T out	Cost/Mass	Cost ratios	Overall heat transfer coefficient
Cooling agents	K	K	\$/MT	Normalized	W/m^2K
Cooling water	298	303	0.05	1.00	150
NaCl Brine	263	273	0.25	3.03	100
$CaCl_2$ Brine	243	253	0.25	3.87	100
Glycol	263	273	0.35	6.42	100
Chilled water	278	283	0.40	8.00	100
Freon	269	270	0.15	65.38	100

9.7: Distillation Properties

To distill the mixture, the boiling point of acetaminophen, acetic acid, and water are necessary. Acetaminophen boils at 420 ^{o}C[45], acetic acid boils at 118 ^{o}C[46] and water at 100 ^{o}C. As the acetaminophen boiling point is significantly above that of acetic acid and water, it is assumed that negligible amounts of acetaminophen will boil. A T-xy graph was created using Aspen's NRTL model; this information will be relevant during separation.

Figure 9.7: T-xy Diagram for Acetic Acid and Water



Section 10: Process Flow Diagrams and Material Balances

All calculations were performed in google sheets, where changing one variable automatically updated and recalculated downstream variables. This was extremely important and valuable as new information improved efficiencies. Furthermore, following process design, cost optimization was achieved effectively with the interconnected sheets. A detailed explanation of the material balance is provided. In the course of performing this balance, many valuable decisions and assumptions were made that dictate overall plant size.

The batch plant was assumed to be operational 80% of the time and the continuous plant 90% of the time. Consultants advised the group to expect the batch plant to require more maintenance because of the larger quantity of moving parts. As such, the batch plant was assumed to be operational for 292 days and continuous for 328.5 days. The remaining days are used for facility maintenance and as a buffer for any unexpected accidents.

With a goal of 30,000 metric tons a year, the batch plant needed to produce 102.74 metric ton a day, while the continuous plant needed to produce 91.32 metric tons a day or 63.42 kg/minute.

10.1: Batch Material Balance

The size of each batch depended on length of time per cycle and this batch time was optimized such that equipment size and quantity minimized costs. The balance for the optimal 2-hour time cycle (A.8) is presented below and as discussed previously, throughout the design process, the 2-hour number could be updated in the spreadsheet and all downstream numbers were automatically recalculated. As a result, 12 batches (24 hours/2-hour batch) are achieved in a day and each batch needs to produce 8.56 metric tons or 8561 kg/cycle.

The plant can be divided into two major sections. The first section addresses the initial reaction and crystallization process, and the second section addresses the dissolution and recrystallization process to purify the acetaminophen. The mass balance is explained by working backwards, starting with the recrystallization (Table 10.1). As the batch process requires seeding to isolate the desirable crystal polymorph, some of the acetaminophen product needs to be withheld from sales and used to seed future batches. It was assumed that the crystallization process would use 5% of the product to seed. By accounting for both crude and recrystallisation, the batch size was divided by 0.9 ultimately demanding 9513 kg of end production. Having identified the desirable amount of product, the next step was to determine the demands of intermediates and reactants.

Of the final product, 5% is used to seed and is dissolved in the solvent; that 5% essentially bypasses the dissolution and recrystallization process. As such, the fluid in the recrystallization only needs to produce 95% of the final cake weight, 9037 kg. As the solubility of acetaminophen at 80 ^oC and 15 ^oC are known as 297.3 g / kg solvent and 43.0 g / kg solvent, respectively, the mass of acetaminophen that can be extracted is the difference between the two or 254.3 g acetaminophen/ kg solvent. Thus, to produce 9037 kg of acetaminophen in the recrystallisation, 35534 kg of solvent is necessary. As the solvent is 8:2 weight ratio acetic acid to water, 28427 kg of acetic acid and 7107 kg of water is required.

It is important to recognize that the solubility curve (Fig 9.1) dictates a maximum yield of 73% following a simple cooling crystallization; this low yield was deemed uneconomical. As such, multiple solutions were considered to reach a yield greater than or equal to 85% as desired by project authors. Initial consideration called for pulling a vacuum to change the composition of the solvent during cooling such that acetaminophen becomes more insoluble. For example, at 15 ^{o}C, 7:3 ratio acetic acid to water has an acetaminophen solubility of 88.18 g/kg solvent, while pure acetic acid has less than 40 g/kg solvent. Thus, starting at a 7:3 ratio at 80 ^{o}C and ending at 10:0 at 15C would drastically improve yield and if the water could be evaporated out while continuing to cool the solution, significantly more acetaminophen could be extracted out. A P-xy diagram for acetic acid and water was generated using the NRTL package in Aspen (A.2) and step-wise composition analysis was conducted. After 4 steps, the pressure reached 0.065 bar, while the weight ratio moved from 30% water to 29.43% water. The boiling point difference between acetic acid and water results in marginal change in solvent composition and with the significant vacuum required, it was concluded that using a vacuum to change the composition was unfeasible.

Another consideration was diluting the solvent to change the composition and decrease the solubility at 15 ^{o}C. Starting at a 7:3 weight ratio, increasing either of the solvents will decrease the solubility. To reach an 8:2 ratio, the total weight increases by 50%, the solubility drops from ~100 to ~50 g acetaminophen/kg solvent and an extra 17 g acetaminophen/kg solvent can be extracted out or ~5%. However, given the 50% increase in equipment size, this was deemed unprofitable. When performing a similar analysis for water addition to reach a 5:5 ratio, the yield would decrease by ~4%.

Ultimately, it was concluded there was no way to improve yield except by recycling the liquid with acetaminophen already dissolved in it. Although it is considered undesirable to recycle in pharmaceutical production due to potential contamination concerns, this project will use Hastelloy vessels and a very healthy purge greater than 25%. In addition, some reports[26] of acetaminophen production use recycle indicating that recycling is already utilised in the industry.

Thus, to obtain the total weight of acetaminophen in the system post crystallization 1, the mass from crystallization 2 is added to the recycle, seeding mass and loss streams to obtain 9895 kg of total extracted cake from crystallization 1 .

As stated above, the 5% acetaminophen used for the seeding process need not be consider in the dissolution and crystallization process. Thus, only 9419 kg of acetaminophen must come from the cake of the crystallization process. As the same temperatures and composition are used here as the recrystallization, 254.3 g acetaminophen/ kg solvent can be extracted. As such, 35165 kg of solvent, 28132 kg acetic acid and 7033 kg water, is used to extract 8943 kg of acetaminophen (plus 476 kg used in the seeding for 9419 kg total). Including loss and recycle, the mass of acetaminophen in the vessel can be determined to be 10931 kg.

The next step is to determine the composition of the vessel prior to the reaction to optimize kinetics and crystal properties. The moles of the p-aminophenol will be equal to that of the post seed moles minus the seeding, 3.15 kmol, and the recycle, which is currently unknown. Iterations will be performed at the end to determine the recycled mass of acetaminophen. Following Jiang et al, pseudo first order reaction conditions were attained by having acetic anhydride in excess of p-aminophenol. This excess reacts with water to form acetic acid and the solution composition impacts nucleation, purity, solubility and crystal size distribution. It was determined that an 8:2

ratio of acetic acid to water would yield the most optimal reaction and reaction conditions which requires a 2.8:1 ratio of acetic anhydride to p-aminophenol (A.1). Via reaction balances, the pre-reactive moles of acetic acid and water can be determined. With the moles and thus mass of water and acetic acid before the reaction known, this provides information on the amount that can be recycled and what needs to be added. Utilizing the 8:2 ratio of acetic acid and water in the recycle, acetic acid was determined to be the limiting factor of the recycle at a mass of 10010 kg, while with the 8:2 ratio, 2503 kg of water is recycled. To obtain the necessary mass of 9160 kg, 6658 kg of water will need to be added each batch. The recycled percentage is 35.6%, the purge amount is clearly at a safe enough level. With the amount of recycle solvent known, the acetaminophen dissolved can be determined. Those moles of acetaminophen will add to the required amount and will reduce the amount of p-aminophenol needed to produce the acetaminophen. This creates an iterative loop in which the recycle and thus dissolved mass of acetaminophen is determined. The numbers described thus far are the optimized solution for a batch process, the inputs come out to 7159 kg of p-aminophenol and 18753 kg of acetic anhydride producing 8562 kg of acetaminophen per batch. Water and acetic acid will need to be added throughout the system, but excess created will be distilled and sold.

Table 10.1: Batch Mass Balance

Acetaminophen Production		**Setting Information**				
		Solvent Weight Ratio		**Solubility**		**Correction Term**
30000	metric tons/year	Acetic Acid	Water	80 C	15 C	kmol
292	operating days	8	2	g acetaminophen/kg solvent		3.6
102.7	metric tons/day			297.3	43.0	Recycled Acetaminophen
2	hours per cycle					
8.562	metric tons/cycle					
8562	kg/cycle					

Reaction and Crystallization	Input		Pre-Reaction		Post-Seed		Recycle	Waste	Cake	
	kg	kmol	kg	kmol	kg	kmol	kg	kg	kg	kmol
Acetaminophen	476	3.1	538	3.6	10931	72.3	538	974	9419	62.3
Acetic Acid			10010	166.7	28132	468.5	10010	18122		
Water	6658	369.6	9160	508.5	7033	390.4	2503	4530		
P-Aminophenol	7159	65.6	7159	65.6						
Acetic Anhydride	18753	183.7	18753	183.7						
Total	33046	622.0	45621	928.0	46096	931.2	13051	23627	9419	62.3
						Split	0.356	0.644		

Recrystallization	Input		Post-Seed		Recycle	Waste	Cake		Sell	
	kg	kmol	kg	kmol	kg	kg	kg	kmol	kg	kmol
Acetaminophen	9895	65.5	11040	73.0	1145	382	9513	62.9	8562	56.6
Acetic Acid	7107	118.3	28427	473.4	21321	7107				
Water	1777	98.6	7107	394.5	5330	1777				
Total	18778	9419.1	46575	940.9	27796	9265	9513	62.9	8562	56.6
				Split	0.75	0.25				

10.2: Continuous Material Balance

The continuous mass balance is performed in a manner that parallels the discussion of the batch process, except that the seeds will already be in the crystallizers (after the initial seeding in startup). The final rate of cake production is known from the project statement to be 63.42 kg/min and thus the material balance works backwards again. Utilizing the same difference in solubility between 80 ^oC and 15 ^oC, 254.3 g acetaminophen/ kg solvent, the necessary solvent needs are 199.49 kg/min acetic acid and 49.87 kg/min water. Identical to the batch process, 75% is the maximum recycled and identification of how much acetaminophen, acetic acid, and water will stay in the system and be removed as waste are the next steps. With 63.42 kg/min removed as the product and 2.68 kg/min removed as waste, 66.10 kg/min comes in from the previous crystallization process. Due to the reaction, an iterative process is also done to determine the recycle. Utilizing the same difference in solubility between 80 ^oC and 15 ^oC, the after reaction amounts of acetaminophen, acetic acid, and water can be determined. Using the same 2.8:1 ratio, the moles of acetic anhydride are also known. Similarly, the final moles of acetic acid and water and the amount produced or consumed in the reaction determines the initial moles. Converting to mass, acetic acid was found to be the limiting agent to the value that can be recycled, limiting it to 35.5%. With the recycle known, the recycle of acetaminophen can be determined and subtracted from the amount of p-aminophenol needed. Iteratively the current solution described is converged upon. As a final result, 52.95 kg/min of p-aminophenol and 138.69 kg/min of acetic anhydride is imputed to obtain 63.42 kg/min of acetaminophen. Again, acetic acid and water are used throughout the system, but also distilled and sold, making the determination of the exact quantities a bit more complex.

Table 10.2: Continuous Mass Balance

Acetaminophen Production	
30000	metric tons/year
328.5	operating days
91.32420091	metric tons/day
0.06341958397	metric tons/min
63.41958397	kg/min

Setting Information				
Solvent Weight Ratio		**Solubility**		**Correction Term**
		80 C	15 C	kmol
		g acetaminophen/kg solvent		0.026
Acetic Acid	Water	297.3	43.0	Recycled Acetaminophen
8	2			

Reaction and Crystallization	Input		Pre-Reaction		Post-Reaction		Recycle	Waste	Cake	
	kg	kmol	kg	kmol	kg	kmol	kg	kg	kg	kmol
Acetaminophen			4.0	0.026	77.3	0.511	4.0	7.2	66.1	0.437
Acetic acid			73.9	1.231	207.9	3.462	73.9	134.0		
Water	49.2	2.733	67.7	3.759	52.0	2.885	18.5	33.5		
4-Aminophenol	53.0	0.485	52.9	0.485						
Acetic anhydride	138.7	1.359	138.7	1.359						
Total	240.9	4.580	337.2	6.860	337.2	6.859	96.3	174.7	66.1	0.437
						Split	0.355	0.645		

Recrystallization	Input		Post-Mixing		Recycle	Waste	Cake = Sell	
	kg	kmol	kg	kmol	kg	kg	kg	kmol
Acetaminophen	66.1	0.437	74.1	0.490	8.0	2.7	63.4	0.420
Acetic Acid	49.9	0.831	199.5	3.322	149.6	49.9		
Water	12.5	0.692	49.9	2.768	37.4	12.5		
Total	128.4	1.960	323.5	6.581	195.1	65.0	63.4	0.420
				Split	0.75	0.25		

10.3: Reasonableness

The individual values for the batch and continuous process were essentially identical when set to produce the same amount of acetaminophen, confirming that both processes are correct. There were minor differences due to the seeding in the batch.

Section 11: Process Descriptions

11.1: Batch

Off-site storages

Off-site storage vessels that can hold up to two weeks' worth of materials are used. The two-week holding amount allows for the plant to continue operating during holidays and when unexpected events occur preventing the delivery of reactants. With 2-hour batch times or 12 batches a day, a total of 168 batches can be produced in 14 days. In terms of the reactants, 1,203,000 kg of p-aminophenol and 3,151,000 kg of acetic anhydride will need to be stored. Due to the reuse of the distillation top stream composed of water and acetic acid, less water and acetic acid will need to be purchased. The exact math for the reuse will be discussed in the distillation section, but 1,119,000 kg of water and 1,405,000 of acetic acid will need to be stored off site to be used. Cone-roof storage tanks are used.

Preheating vessels

To reduce the batch time, the liquid will be heated in a heat exchanger and stored in an insulated vertical pressure vessel until the batch is ready to begin. Preheating was done to avoid the slow heating in the jacketed reactor vessel and adding storage tanks was significantly cheaper than staggering more reactors. There will be two vessels, one for acetic anhydride and another for the water plus recycle. To minimize utility cost and heat exchanger size, the fluid will spend the maximum time in the preheater as determined by the optimal batch time of 2 hours. As such, the fluid is heated for 90 minutes, and 10 minutes is afforded to pumping to the reaction vessel. The remaining 20 minutes can be used to clean the equipment or otherwise integrated into heating time awarding smaller heat exchanger. Although potentially unnecessary, both vessels will contain an agitator to ensure the temperature is evenly distributed within. Both heat exchangers will be double-pipe heat exchangers and use 5 atm steam to achieve a relatively small heat exchanger. After optimization, the water plus recycle vessel will contain 19,709 kg of material heated to 46 ^oC using a 7.9 m^2 heat exchanger. Note that the recycled liquid is used in the Nutsche filter at 15 ^oC, thus making the input temperature 19.7 ^oC rather than 25 ^oC room temperature. The acetic acid vessel will contain 18,753 kg of material heated to 46 ^oC using a 3.3 m^2 heat exchanger.

As the pre-heating heat exchanger sizes are relatively small, it is suggested that further analysis be done to determine if larger heat exchangers can eliminate the need for the preheating vessels.

Reaction vessel

Reaction was modeled as an irreversible pseudo first order reaction. A 10-second time step model was used with temperature starting at 80 ^oC to produce a smooth reaction profile curve. As a function of the temperature and the fraction that has already been reacted, the first order rate law can predict the rate of reaction. The enthalpy of formation, change in fraction of conversion, and concentration determine the energy consumed by the reaction. Utilizing the heat capacity of the entire mass of liquid in the reactor, the temperature drop can be determined. In the next time step, using the rate of change of fractional conversion and temperature, the new fractional conversion and temperature can be determined. This methodology was repeated until 99.9% of the p-aminophenol had been reacted. As an endothermic reaction, the reactor required continual heating to be maintained at 80 ^oC once everything had reacted. To ensure the reaction proceeds smoothly, an agitator is required.

The second reaction for acetic anhydride and water was modeled as an irreversible first order reaction. The same process as the first reaction was performed, except that the fractional conversion of acetic anhydride accounted for the consumption by the first reaction. As such, the fractional conversion included the consumption of acetic anhydride in both the first and second reactions when calculating the new reaction rate for the second reaction. As the second reaction proceeds at a rate much slower than the first reaction, the assumption that the acetic anhydride will remain in excess for the duration of the first reaction is valid. The second reaction is highly exothermic and thus optimization was performed by adjusting the initial temperature such that the maximum vessel temperature never exceeded 80 ^oC. It was also pertinent to ensure this maximum temperature was reached as the second reaction was nearing completion, so all the p-aminophenol and acetic anhydride have been consumed and acetaminophen and acetic acid have been made. Following the 8:2 weight ratio of acetic acid to water solubility curve, it is expected that all of the acetaminophen is dissolved in the solution at this point.

Figure 11.1: Temperature across reaction profile

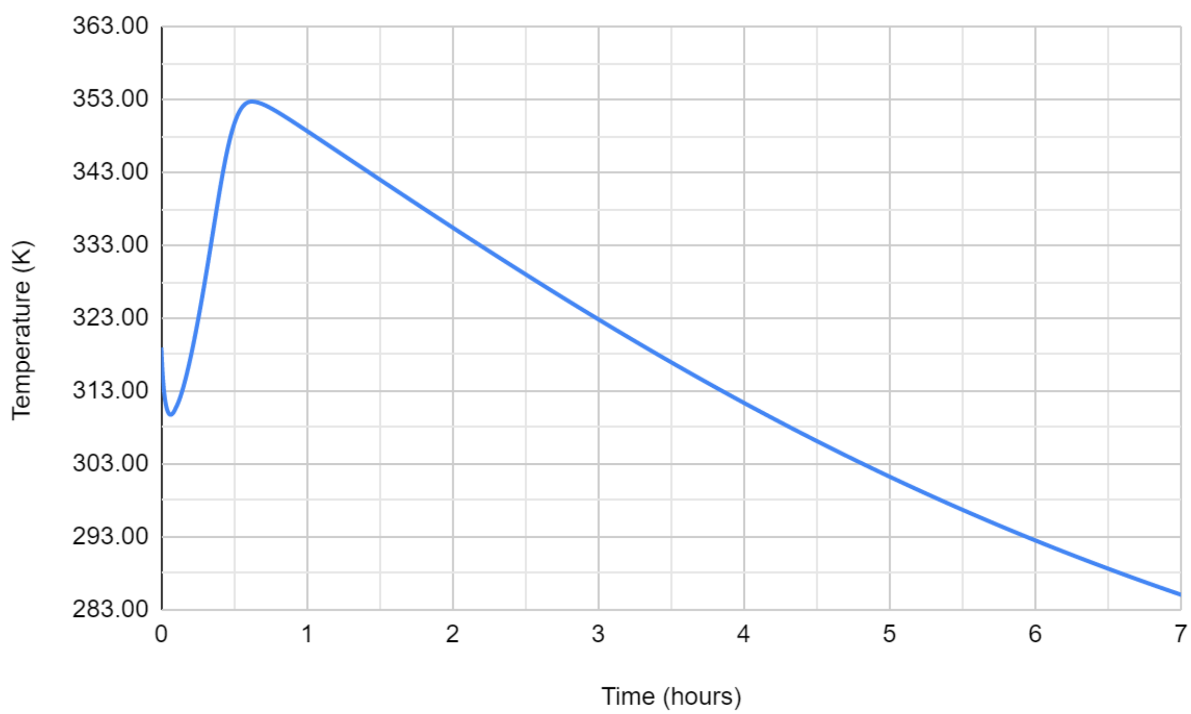
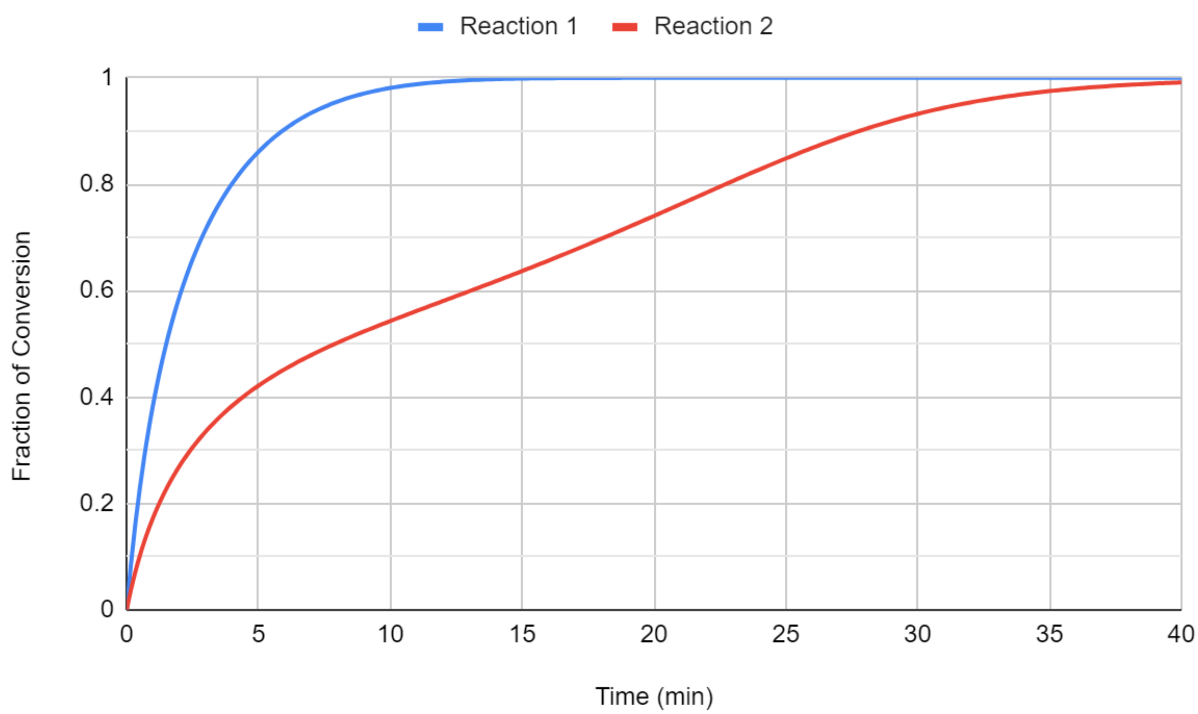


Figure 11.2: Conversion for both reaction 1 and reaction 2



For crystallization, due to the extreme amount of energy needed to cool the fluid, utilizing a heat exchanger, and completing crystallization in another vessel was considered. However, fears of crystallization in the pipes prevented this idea from moving forward. Rather than creating another vessel, the fluid will be cooled back to 15 ^oC in the same vessel and staggering will be utilized to achieve the 2-hour batch time. Initially, chilled water was considered and the area of the jacket was approximated through designing the reactor vessel to be 85% full as a 2:1 height to diameter ratioed cylinder. The jacket area was then estimated to be the area of the base of the cylinder and the 85% of the sidewall as that was the area the fluid volume. The temperature difference was initially modeled as the difference between 10 ^oC, the hottest the chilled water gets to, and the temperature of the vessel at the time step. As a result, the cooling rate in watts can be calculated and changes as the vessel temperature decreases towards 15 ^oC. A cutoff was set at 15 ^oC and the time was recorded. Log mean temperature difference utilizing the input and output temperature of the cooling agent and the vessel temperature was eventually used.

The timing of the cooling agent was optimized, and it was found that this had relatively negligible effects on the initial temperature nor the time it took to cool to 15 ^{o}C with a max temperature of 80 ^{o}C. The sooner cooling begins, the higher the initial temperature needed to be while the time was minimized - this took place over a range of 4 ^{o}C and 4 minutes. As this had little impact, a middling point when reaction 1 was 90% complete was chosen. This coincided with reaction 2 ramping up and the temperature quickly climbing as demonstrated in Figure 11.1.

Next, the energy to crystalize the acetaminophen from the solution, 27600 J/mol, was considered. Crystallization energy was modeled to commence after reaching the max temperature of 80 ^{o}C and seeds were added. Although seeding will happen once the vessel has been cooled a couple degrees to prevent the seeds from dissolving, for simplicity, it was assumed crystallization starts from the peak temperature; this has relatively negligible effects on the amount of energy needing removal. Using the temperature from each time step, the solubility as a function of temperature, can be determined. The difference in solubility between time steps is the amount of acetaminophen that has been crystallized and the energy it took to crystallize it. This difference was removed from the current time step, thus slowing the rate of cooling for future time points. The introduction of crystallization caused fluctuations in temperature and created errors in the sheet if those fluctuations were uncontrollable. But with small time steps, the initial fluctuations were dampened out within the first minute.

After the model was complete, optimization was performed to determine the cooling agent and as discussed in Section 9, only the NaCl brine and $CaCl_2$ brine were considered. The increased temperature difference of the $CaCl_2$ brine decreased the amount of time it took to cool to 15 ^{o}C.

The cost saving from less equipment eclipsed that of the increased cost of the cooling agent making it the ideal component.

Table 11.1: Optimization of equipment cost vs operating cost

Cooling Agent	Equipment Staggered	Equipment cost	Operating cost	Comparison
NaCl Brine	5	$8,636,000	$244,000	$9,123,000
$CaCl_2$ Brine	4	$6,908,000	$315,000	$7,538,000

In totality, including the seeds, the vertical pressure reactor vessel needs to handle 46,096 kg of material. With 20 minutes to input the reactants, 396 minutes to react and cool the fluid, and 15 minutes to pump the fluid out, a total of 431 minutes or 7.2 hours was needed. To get 2-hour batches, four of this equipment unit are needed and the extra 12 minutes per batch serves as a control. For future optimization, it is proposed to consider using faster pumps to reduce the time and eliminating the extra time per batch. Internal coils can also be considered to cool the vessel at a quicker rate.

Storage Vessel

The slow Nutsche Filter throughput necessitated a holding vessel between the reactor and the Nutsche Filter as a more economical approach considering the lack of a jacket. The vessel will still need to contain an agitator to prevent the crystals from settling and ensure good transfer to the filter. The process of transferring the fluid into the Nutsche filter is approximated to take two hours as the fluid slowly drains through the filter. As such, the vessel is modeled to receive the fluid from the reactor in 15 minutes and simultaneously start transferring the fluid out over the course of 2 hours. This throughput permits the use of just one holding vessel. As demonstrated, rather than increasing the transfer out time of the reactor to 2 hours, and increasing the number of reactor vessels to 5, the number of reactor vessels can be kept at 4 and a cheaper holding vessel is used. However, if the filter requires less time that this estimation, it may become more economical to remove the storage vessel.

Nutsche Filter

A nutsche filter was selected as the filtration process to remove the crystallized acetaminophen, 9419 kg of solid, from the solvent. This was selected because the filter can process a large amount of fluid in a reasonable time frame and can be used to dry the cake as well, thus reducing the need for additional equipment. The basic steps consist of feeding the fluid through the filter, washing with an identical solvent, 8:2 ratio of acetic acid to water, washing with water, drying and transferring the cake out. Both washes will contain liquid equal to half the mass of the crystals, 4710 kg, and be cooled to 15 ^{o}C prior to washing to minimize the chance of acetaminophen being dissolved and removed by the stream. In terms of calculations, the model assumes that a negligible amount of acetaminophen is removed but the wash will still be fed to the distillation column to remove any trace amounts for clean recycle. A consultant estimated the filtering and drying process of our scale to take about 11 hours. For this first filtration, the cake will be recrystallized, as such it does not need to be perfectly dried. As exact filter specification could not be obtained, an assumption was made that the fluid will take around 2 hours to filter, 0.5 hours for each wash and 8 hours to fully dry and transfer out. However as recrystallization is performed in the next step, the crystals do not need to be fully dried out and 1 hour was utilized for the drying and transfer out process. With a 2-hour batch time, 2 nutsche filters will need to be staggered with the remaining time used to dry the cake as much as possible.

The nutsche filter discharge will be sent to two different holding vessels. Initially, for the fluid the acetaminophen is filtered out of, it will be sent to a holding cell used for recycling. The acetaminophen is saturated in the fluid at that temperature, by recycling this undiluted liquid, the maximum amount of acetaminophen gets recycled, thus requiring less reactants. The fluid from the washes is sent to a holding vessel prior to the distillation column to control the timing of transfer into the distillation process.

Due to the long transfer time, 30 minutes, heat exchangers will be used to directly cool the wash fluid before using them, no holding cell will be necessary. The 8:2 wash will utilize part of the top stream of the distillation combined with procured acetic acid at 76 ^{o}C (likely lower due to heat exchange with the environment), and the water wash will come directly from the off-site water tank at a standard temperature of 25 ^{o}C. The cooling agent was not optimized due to the relatively low cost of the unit, and chilled water is used. The 8:2 wash will require a 134 m^2 heat exchanger while the water wash will require an 89 m^2 heat exchanger.

Recycle 1

As stated in the previous section, the fluid with acetaminophen dissolved in it is held in a vertical pressure vessel used for recycling. For simplicity, even though fluid will stick to the cake and not all of it will make it into the vessel, it remains a conservative estimate as larger equipment will be needed. This vessel will handle 36,678 kg of fluid per batch. As determined in the mass balance, 13,051 kg of material will be recycled, that will enter a mixer with the necessary water and be heated and deposited into a preheating vessel as described previously. The remaining 23,627 kg will be sent to the distillation column to extract as much acetic acid and water for sale as possible.

Preheating solvent

Much like preheating the reactants for the reactor, a vertical pressure vessel will be used to preheat the solvent to 80 ^{o}C for the recrystallization process. The fluid will be heated in a heat exchanger and slowly fed to the vessel over the course of 90 minutes. 15 minutes will be needed to transfer the fluid into the vessel and a 15-minute surplus for cleaning is awarded. If found to be superfluous, this can otherwise be used to increase the heating time and reduce the size and cost of the heat exchanger. An agitator will ensure the temperature is even throughout the liquid.

The fluid will enter at a temperature of 30 ^{o}C and this is a combination of the acetic acid at standard temperature, the 15 ^{o}C recycle, and the 107 ^{o}C acetic acid and water combination from the distillation tower. This will be heated to 80^{o}C as there will be no reaction to heat the fluid from a lower temperature. A double-pipe heat exchanger will be used with 5 atm steam and 27.6 m^2 of area is required. Again, this vessel may not be necessary depending on the amount of time it takes to dissolve the cake. It may be more economical to use a larger heat exchanger and directly deposit the fluid into the dissolving vessel if time is not a concern. But for a more conservative approach a preheating vessel was used.

For further optimization, the dissolving process may release enough heat such that the preheating solvent does not need to reach 80 ^{o}C. On the other hand, the fluid needs to travel through the granular activated carbon without crystallization, so temperatures above 80 ^{o}C may be needed to ensure the fluid is still at 80 ^{o}C when it reaches the crystallization vessel. But for simplicity, the solvent is heated to 80 ^{o}C.

Dissolver

The dissolving vessel is a vertical pressure that will receive the solvent from the preheating vessel and the cake from the nutsche filter which will sum up to a mass of 46,099 kg. There was no data on the rate acetaminophen dissolves at, but videos and lab experiments demonstrate that it is not an unusually long period of time. As such, the maximum amount of time without staggering is assumed to be sufficient. With 30 minutes for transfer in – the solid transfer from the nutsche filter is assumed to be rather slow - and 20 minutes transferring out, slower than usual as this is through the granular activated carbon, a total of 70 minutes is allotted to dissolving the cake and consultants confirmed this appeared to be a sufficient time frame. When designing the plant, care should be taken to check that the time frame is sufficient, else reducing transfer time or staggering may be necessary.

Granular Activated Carbon

The granular activated carbon column is a vertical pressure vessel used to remove impurities from the stream. Inconsistent isotherms could be sourced online and very little was available on what impurities might be present. Consultants advised that the GAC properties and quantity requires empirical analysis and attempting to scale from similar small compounds will not necessarily be a good approximation. As such, very conservative estimations of activated carbon needs are priced here and kept consistent with continuous.

With a transfer time of 20 minutes, this will be the amount of time the column has to purify the stream. The stream will contain 46,099 kg of material with a density of 1,328 kg/m3, resulting in a volumetric flow rate of 61.3 ft3/min. As recommended by Seider Textbook and considered conservative, the fluid should progress 1 ft/min in the column. The diameter and the height will be set as twice the diameter plus 2 ft. As such a total volume of 1,289 ft^3 is required of the vessel. With a density of 125 lb/ft^3[47], assuming spheres which have a packing density of 0.74, and that vessel is 85% full, 101,000 lb of activated carbon is used to fill the vessel. As an estimate, 1% of the mass flowing through it is used up of the activated carbon, so the activated carbon can last 99 batches or 8.25 days. It is impossible to unload and reload the column in a two-hour time frame, so two columns will be used. While one is being used, the other is being loaded and unloaded. The

100-minute gap between batches will allow for enough time to switch the column. In terms of the calculations, no material is assumed to be removed here as impurities were not modeled.

A vessel to store the granular activated carbon was not included as standard operating procedure was not set. Recognizing this cost would be identical for both continuous and batch, it was reasonable to omit.

Crystallizer Vessel

The recrystallization vessel, an autoclave vessel, will behave in much the same way as the crystallization part of the reactor vessel. A jacket and agitator will be necessary to ensure efficient heat transfer and prevent crystals from settling when transferring the fluid. The model for the calculation is identical to that of the reactor vessel, except with no reaction present, essentially the energy removed is calculated based on the cooling agent and area of the jacket. For simplicity, seeding is assumed to start at the very start while the fluid is still at 80 ^{o}C, even though realistically the fluid will be slightly cooled first to prevent the seeds from dissolving. Larger time steps of 5 minutes were taken here as without the reaction, the model is much less sensitive. Based on the optimization and finding that $CaCl_2$ brine worked best for the first reactor vessel, the same cooling agent is assumed to function best here as well. As such, the vessel requires 20 minutes to transfer the fluid in, 355 minutes to cool and crystalize, and 15 minutes to transfer out for a total of 390 minutes. This would require staggering for 4 equipment units with 22 minutes between batches in a vessel. Again, that time can be used to clean the vessel or as leeway in case any accidents occur. Future optimization may involve bringing this time below 360 minutes by adding internal coils or working with different start and end temperatures, as to reduce one whole piece of equipment.

Holding Vessel

Similar to between the reactor vessel and the first nutsche filter, a vertical pressure vessel was used to hold the liquid to slowly transfer into the nutsche filter because it was cheaper than another reactor vessel. The same thing will be done here.

Nutsche Filter

A nutsche filter will be used here for the same reason as the first. In addition to the filtering and washing, this filter will also dry the acetaminophen so that it can be stored and sold. Note, the approximate breakdown estimated time scales are 2 hours to filter, 0.5 hours for each wash and 8 hours to fully dry and transfer out. The filter will remove 9,513 kg of acetaminophen, this is slightly higher than the first nutsche filter because the seeding adds more acetaminophen than is lost in the purged stream. The first wash will consist of 4,756 kg, half the mass of acetaminophen, of 8:2 ratio acetic acid to water, while the second wash contains 4,756 kg of water. The remaining wet cake is then heated and dried and transferred out over the course of 8 hours. Identical to the first nutsche filter, the discharge with dissolved acetaminophen will be used in the recycle to maximize acetaminophen recycled and thus yielded. The wash discharge is likewise sent to be distilled.

Heat exchangers will be used to cool the wash fluid to 15^{o}C before they are used. The 8:2 wash will utilize fluid from the distillation column mixed with acetic acid, resulting in a temperature of 76^{o}C while the water comes from the off-site storage tank assumed to be at a standard temperature of 25^{o}C. The cooling agent was not optimized due to the relatively low cost of the unit and chilled water is used. The 8:2 wash will require a 135 m2 heat exchanger while the water wash will require a 90 m2 heat exchanger. It may be possible to double up with the pump and heat exchanger of the first nutsche filter as both processes only occupy 30 minutes of the 2 hours, but due to concerns that the required 30 minutes may overlap and the relatively low cost of the equipment units, the process units were kept separate. Optimization may be possible here to reduce units and cost.

Recycle 2

The second recycle is contained in another vertical pressure column with the capacity to hold 37,062 kg. Both the inputs and outputs function on a two-hour time scale, so the vessel will not be expected exceed this capacity. 27,796 kg will be sent to a mixer to be combined with acetic acid and water from the distillation process and pure procured acetic acid to be heated and deposited into the preheating vessel for the recrystallization process. The other 9,265 kg of material will be taken into the distillation column to extract acetic acid and water for sale.

Distillation

The distillation process will involve a simple batch distillation. The process will be approximated with a vertical pressure vessel with 3 times the height than diameter and two heat exchangers, one for heating and evaporating and the other for condensing. The distillation column will receive fluids from three sources, both recycle vessels and the vessel containing the washes, for a total of 51,824 kg — 1,355 kg of acetaminophen, 32,802 kg of acetic acid, and 17,666 kg of water. Acetaminophen has a high boiling point at 420 ^{o}C compared to water, 100 ^{o}C, and acetic acid, 118 ^{o}C. It is reasonable to assume the acetaminophen will not evaporate into the top product and as water and acetic acid evaporates, acetaminophen will become concentrated in the bottom's product. As much of the acetic acid and water is saved as possible, but the bottoms are not allowed to exceed 200 g acetaminophen/kg solvent, and this is to ensure the acetaminophen stays in a slurry for easy transport to waste. The bottoms will require 6,777 kg of solvent while the distillate will contain the remaining 43,691 kg. Utilizing the T-xy diagram from the Section 9, a mass balance was performed to determine the composition of the solvent in both sections. A necessary temperature of 107 ^{o}C was required, and the top stream was 0.63 mass fraction acetic acid with the remaining being water. Impurities were not modeled here.

The transfer in time is modeled to take 10 minutes with 20 minutes to transfer out the separated fluid. Thus, 90 minutes is awarded for the distillation process but as the condensation cannot occur until the fluid starts evaporating, the entire 90 minutes will not be utilized. For this model, only 60 minutes was used for both the heating and cooling heat exchangers. The heating heat exchanger will utilize 5 atm steam as the 152 ^{o}C is sufficient to heat the fluid to 107 ^{o}C. 794 m^2 of area will be required to heat at the desired rate. The cooling heat exchanger will utilize NaCl brine, the extra 20^{o}C of temperature difference for $CaCl_2$ brine has negligent benefit when the temperature difference is already over 100 ^{o}C to warrant the extra cost. This requires 1489 m^2 of area. As these areas exceed 200 m^2, a fixed head heat exchanger is used for both.

Both the distillate and bottoms are allowed to remain as 107 ^{o}C liquids, they will either cool off naturally with heat exchange with the environment or be cooled in a heat exchanger.

8:2 storage

Throughout the process, 8:2 ratio of acetic acid to water is required at a capacity of 18,350 kg per batch. Some of the distillate from the distillation column is repurposed for this rather than sold, but with 0.63 acetic acid, it must be supplemented with glacial acetic acid. As discussed in the offsite storage section, acetic acid is bought and stored there to be used in this process. To achieve the correct weight and mass fraction, 9,988 kg of the distillate is repurposed for this while 8,362 kg of acetic acid is added. This is stored in a vertical pressure vessel designed to hold 18,350 kg.

Off-site storage

Three main off-site storage vessels will be necessary postproduction. One for acetaminophen, acetic acid plus water distillate, and the bottoms waste. Similar to the receiving off-site storage tanks, these also store two weeks of production to accommodate holidays or unexpected events. A maximum of 168 batches can be made in this time, thus requiring the storage of 1,438,000 kg of acetaminophen, 5,662,000 kg of 63% acetic acid with water, and 1,366,000 of waste. Large, cone-roof storage tanks are used. The acetic acid and water solution and waste will be transferred at 107°C from the distillation column and will be allowed to naturally cool. Consideration was given to heating the tanks to prevent freezing, but with a location of India, the tanks will not get cold enough for the fluid within to freeze.

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Figure 11.3: PFD Batch

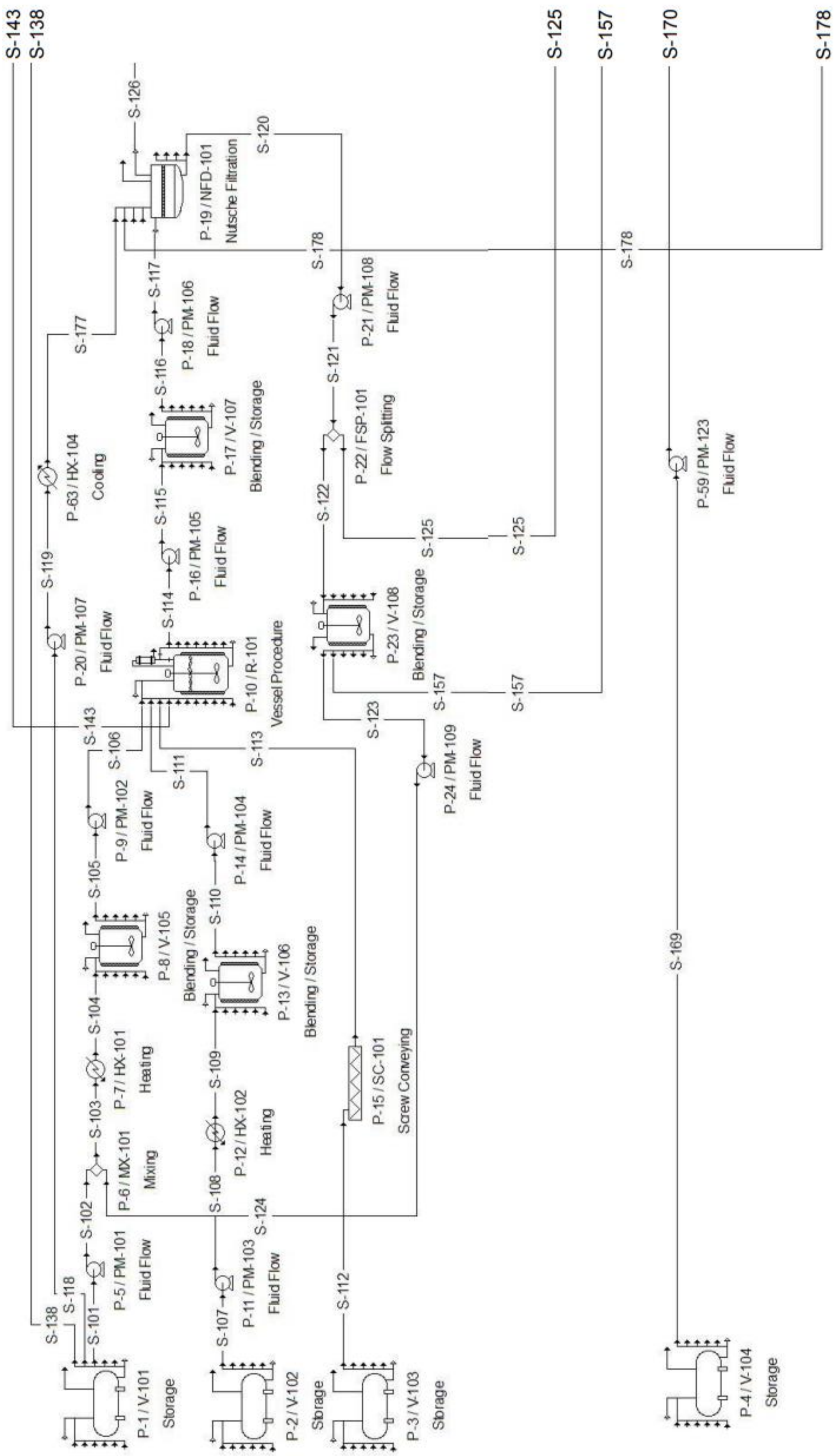


Figure 11.3: PFD Batch Cont.

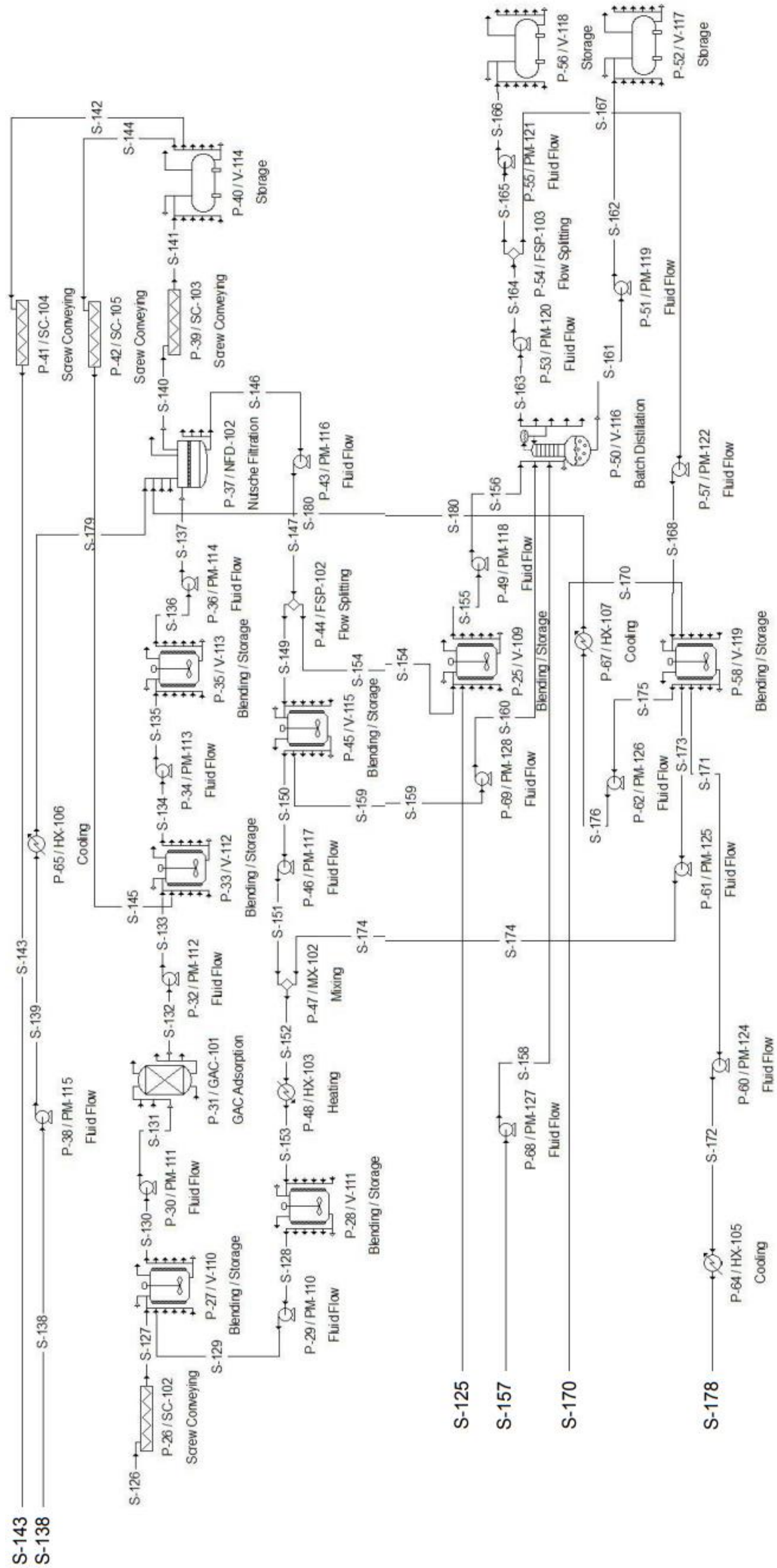


Table 11.2: Batch Stream Properties

		S-101	S-102	S-103	S-104	S-105	S-106	S-107	S-108	S-109	S-110
State of Matter		L	L	L	L	L	L	L	L	L	L
Mass	kg/cycle	6658	6658	19709	19709	19709	19709	18753	18753	18753	18753
Acetaminophen	kg/cycle			538	538	538	538				
Acetic Acid	kg/cycle			10010	10010	10010	10010				
Water	kg/cycle	6658	6658	9160	9160	9160	9160				
P-aminophenol	kg/cycle										
Acetic Anhydride	kg/cycle							18753	18753	18753	18753
Mol	kmol/cyc	370	370	679	679	679	679	184	184	184	184
Time	min	90	90	90	90	10	10	90	90	90	10
Temperature	C	25	25	19.7	46	46	46	25	25	46	46
Density	kg/m^3	1000	1000	1044	1044	1044	1044	1080	1080	1080	1080
Volumetric flow	m^3/min	0.074	0.074	0.209	0.209	1.887	1.887	0.192	0.192	0.192	1.736

	S-111	S-112	S-113	S-114	S-115	S-116	S-117	S-118	S-119	S-120	S-121
State of Matter	L	S	S	L	L	L	L	L	L	L	L
Mass	18753	7159	7159	46096	46096	46096	46096	4710	4710	46096	46096
Acetaminophen				10931	10931	10931	10931			1511	1511
Acetic Acid				28132	28132	28132	28132			31900	31900
Water				7033	7033	7033	7033	4710	4710	12685	12685
P-aminophenol		7159	7159								
Acetic Anhydride	18753										
Mol	184	66	66	931	931	931	931	261	261	1245	1245
Time	10	20	20	15	15	120	120	30	30	180	180
Temperature	46	25	25	15	15	15	15	25	15	15	15
Density	1080	1130	1130	1342	1342	1342	1342	1000	1000	1056	1056
Volumetric flow	1.7364	0.316	0.316	2.289	2.289	0.286	0.286	0.157	0.157	0.242	0.242

Table 11.2: Batch Stream Properties Continued

	S-122	S-123	S-124	S-125	S-126	S-127	S-128	S-129	S-130	S-131
State of Matter	L	L	L	L	L	L	L	L	L	L
Mass	36677	13051	13051	9419	9419	9419	36680	36680	46099	46099
Acetaminophen	1511	538	538		9419	9419	1145	1145	10565	10565
Acetic Acid	28132	10010	10010	3768			28427	28427	28427	28427
Water	7033	2503	2503	5651			7107	7107	7107	7107
Mol	869	309	309	376	62	62	875	875	938	938
Time	120	90	90	60	30	30	15	15	20	20
Temperature	15	15	15	15	15	15	80	80	80	80
Density	1068	1068	1068	1012	1260	1260	1057	1057	1328	1328
Volumetric flow	0.2862	0.1358	0.1358	0.1552	0.2492	0.2492	2.3138	2.3138	1.7353	1.7353

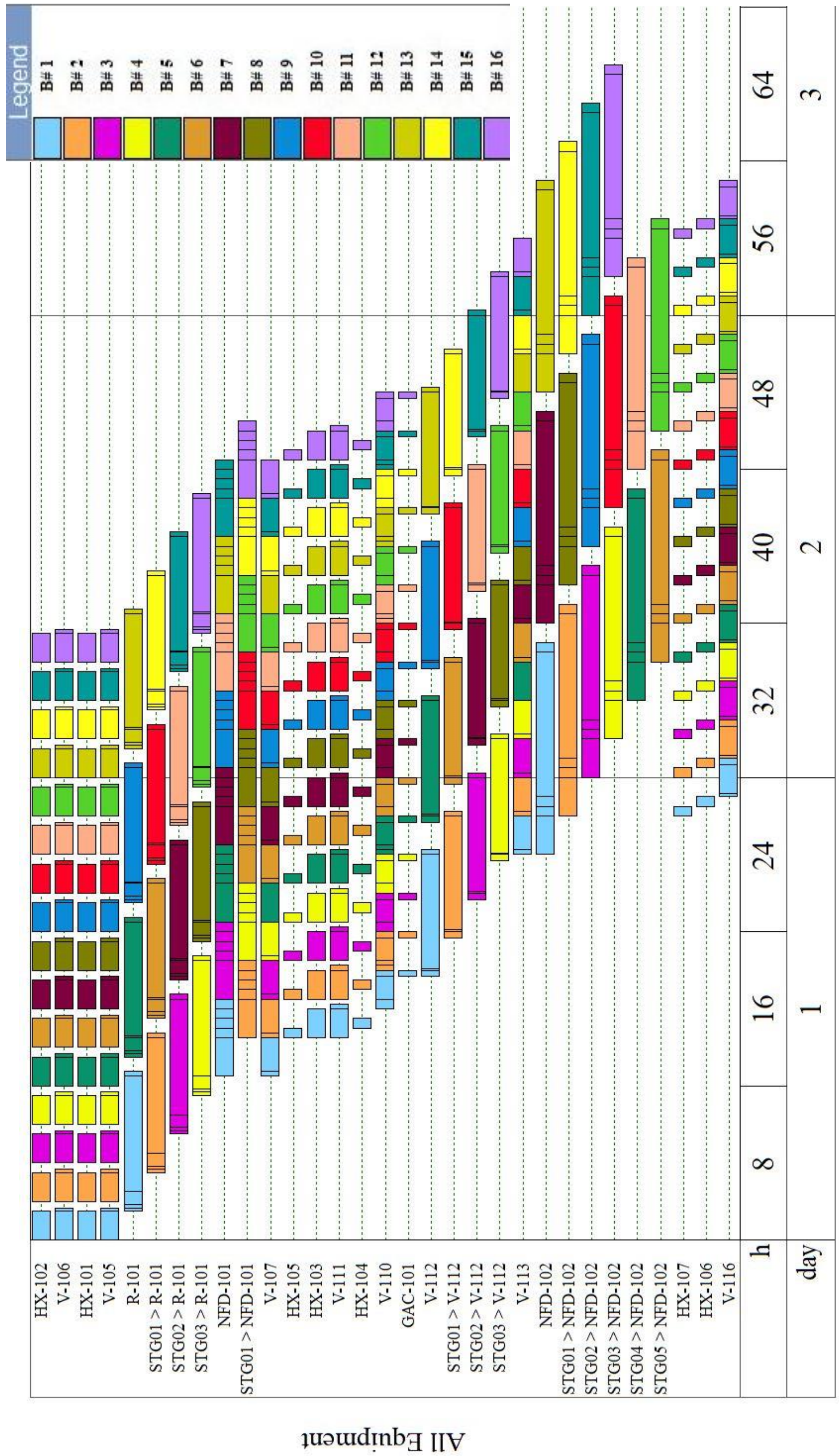
	S-132	S-133	S-134	S-135	S-136	S-137	S-138	S-139	S-140
State of Matter	L	L	L	L	L	L	L	L	S
Mass	46099	46099	46575	46575	46575	46575	4756	4756	9513
Acetaminophen	10565	10565	11040	11040	11040	11040			9513
Acetic Acid	28427	28427	28427	28427	28427	28427			
Water	7107	7107	7107	7107	7107	7107	4756	4756	
Mol	938	938	941	941	941	941	264	264	63
Time	20	20	15	15	120	120	30	30	30
Temperature	80	80	15	15	15	15	25	25	15
Density	1328	1328	1342	1342	1342	1342	1000	1000	1260
Volumetric flow	1.7353	1.7353	2.3138	2.3138	0.2892	0.2892	0.1585	0.1585	0.2517

	S-141	S-142	S-143	S-144	S-145	S-146	S-147	S-149	S-150
State of Matter	S	S	S	S	S	L	L	L	L
Mass	9513	476	476	476	476	46575	46575	37062	27796
Acetaminophen	9513	476	476	476	476	1527	1527	1527	1145
Acetic Acid						32233	32233	28427	21321
Water						12815	12815	7107	5330
Mol	63	3	3	3	3	1258	1258	878	658
Time	30	5	5	5	5	180	180	120	90
Temperature	15	25	25	25	25	15	15	15	15
Density	1260	1260	1260	1260	1260	1056	1056	1068	1068
Volumetric flow	0.2517	0.0755	0.0755	0.0755	0.0755	0.2450	0.2450	0.2892	0.2892

Table 11.2: Batch Stream Properties Continued

	S-151	S-152	S-153	S-154	S-155	S-156	S-157	S-158	S-159	S-160
State of Matter	L	L	L	L	L	L	L	L	L	L
Mass	27796	36680	36680	9513	18932	18932	23626	23626	9265	9265
Acetaminophen	1145	1145	1145				974	974	382	382
Acetic Acid	21321	28427	28427	3805	7573	7573	18122	18122	7107	7107
Water	5330	7107	7107	5708	11359	11359	4530	4530	1777	1777
Mol	658	875	875	380	757	757	560	560	219	219
Time	90	90	90	60	10	10	10	10	10	10
Temperature	15	30.0	80	15	15	15	15	15	15	15
Density	1068	1057	1057	1012	1012	1012	1068	1068	1068	1068
Volumetric flow	0.2892	0.3856	0.3856	0.1567	1.8711	1.8711	2.2125	2.2125	0.8677	0.8677
	S-161	S-162	S-163	S-164	S-165	S-166	S-167	S-168	S-169	S-170
State of Matter	L	L	L	L	L	L	L	L	L	L
Mass	8133	8133	43691	43691	33703	33703	9988	9988	8362	8362
Acetaminophen	1355	1355								
Acetic Acid	5164	5164	27637	27637	21319	21319	6318	6318	8362	8362
Water	1613	1613	16054	16054	12384	12384	3670	3670		
Mol	184	184	1351	1351	1042	1042	309	309	139	139
Time	20	20	20	20	20	20	20	20	10	10
Temperature	107	107	107	107	107	107	107	107	25	25
Density	1227	1227	1019	1019	1019	1019	1019	1019	1030	1030
Volumetric flow	0.3313	0.3313	2.1443	2.1443	1.6541	1.6541	0.4902	0.4902	0.8118	0.8118
	S-171	S-172	S-173	S-174	S-175	S-176	S-177	S-178	S-179	S-180
State of Matter	L	L	L	L	L	L	L	L	L	L
Mass	4710	4710	8884	8884	4756	4756	4710	4710	4756	4756
Acetaminophen										
Acetic Acid	3768	3768	7107	7107	3805	3805		3768		3805
Water	942	942	1777	1777	951	951	4710	942	4756	951
Mol	115	115	217	217	116	116	261	115	264	116
Time	30	30	90	90	30	30	30	30	30	30
Temperature	76.1	76.1	76.1	76.1	76.1	76.1	15	15	15	15
Density	1024	1024	1024	1024	1024	1024	1000	1024	1000	1024
Volumetric flow	0.1533	0.1533	0.0964	0.0964	0.1549	0.1549	0.1570	0.1533	0.1585	0.1549

Figure 11.4: Equipment Occupancy Chart



11.2 Continuous

Off-site storage

Identical to the batch process, the off-site storage tanks are required to hold two weeks of material. 1,067,000 kg of p-aminophenol and 2,796,000 kg of acetic anhydride will need to be stored. Due to the reuse of the distillation top stream composed of water and acetic acid, less water and acetic acid will need to be purchased. The exact math for the reuse will be discussed in the distillation section, but 993,000 kg of water and 1,143,000 of acetic acid require off-site storage. Large, cone-roof storage tanks are used. These numbers are slightly lower than that of the batch process because the continuous process will be operating for 36.5 days more over the course of the year, so two weeks of full operation requires less reactants and produces less product. Not requiring seeding slightly decreases material required.

Preheating heat exchangers

Unlike batch, there is not a need for preheating vessels to control timing, instead, the fluid can be fed through a heat exchanger and deposited directly into a vessel for reaction. The water is mixed with the 15 ^{o}C recycle, resulting in a flow rate of 145.6 kg/min of 19.7 ^{o}C fluid. As later determined in the following reaction section (CSTR), the material must be heated to 53.7 ^{o}C. With this temperature, 5 atm steam will be used in a 7.05 m^2 heat exchanger. 25 ^{o}C acetic anhydride will be transferred in from the off-site storage tank and heated to the same temperature using the same heating agent; an area of 3.14 m^2 will be necessary. As both heat exchangers are relatively small, double-pipe heat exchangers are used.

The p-aminophenol will be transferred to the reactor using a screw feeder at a rate of 52.95 kg/min. The p-aminophenol will not be heated, and the energy release of the dissolution was not considered. As such the preheating temperature for the fluids may need to be adjusted slightly.

CSTR

Continuous stirred tank reactors (CSTR) and plug flow reactors (PFR) were both modeled for this reaction at 80ºC. The amount of time for 99.7% conversion of reaction 1 is relatively low at 17 minutes with 2 CSTR's. As PFR's are relatively difficult to construct such that there is no axial mixing and heat exchange becomes complex as radial mixing is limited, the main advantage of using a PFR, the decreased time, is relatively unimportant. The CSTR model was selected.

For reaction 2, as the acetic anhydride is also consumed in the first, faster reaction, where the batch model started with a 2.8 ratio of p-aminophenol and subtracted p-aminophenol out of that pool as the first reaction occurred, the CSTR model will only contain 1.8 ratio of p-aminophenol, the excess. As a limitation of the CSTR formula, this will cause the second reaction to be modeled to react slower than expected. But as it is slower, this means the model is more conservative making it an acceptable assumption. With the inclusion of the second, slower reaction, although it requires a longer amount of time, CSTR were still preferred.

In a batch reactor, due to the slow cooling, essentially 100% of both reactions occur. In the continuous reactor, fractional conversion depends on CSTR time. The main concern was the unreacted acetic anhydride could continue to react further down the line and causes issues with heating the liquid unexpectedly, as such the conversion versus the temperature increase the unreacted fraction can cause to the fluid was found. The molar flow rate of the excess acetic anhydride is 14.6 mol/s and the reaction releases 58,900 J/mol, releasing a total of 857,311 J/s. The heat capacity was found to be 2.19 J/gK as a weighting of all the components in the stream with a flow rate of 5,620 g/s meaning the fluid can absorb 12,320 J/sK. The total reaction can heat the fluid 69.6 K, to limit it below a 2 K increase, a fraction of conversion of 97% was selected as the end point. As the CSTR model underestimates the speed reactions can occur in the pipe, and that the reaction can occur while the fluid is being cooled and crystallized, it is expected the actual final conversion to be higher than 97%.

The number of CSTR's and timing needs for 97% conversion were recorded and the heat exchange for the CSTR was characterized. The conversion of both reactions in each reactor was determined and overall reaction enthalpy indicated that cooling would need to be applied. For the first CSTR, the reactants are introduced at a temperature below 80 ^oC, such that the reaction will heat the material to 80 ^oC, this will be used in lieu of a cooling jacket to save on utility and jacket cost. For every CSTR afterwards, chilled water will flow through the jacket to cool the vessel at a rate such that the vessel remains at 80 ^oC. Utilizing the flow rate and residence time, the volume of the vessel can be determined; and assuming an 85% full 2:1 ratio of height to diameter, the area of the jacket can be determined. Using chilled water and log mean temperature difference, the maximum cooling rate is determined. The cooling required of a vessel cannot exceed this maximum and it was found this occurred when the quantity of CSTR's exceeded 4 because not enough of the exothermic reaction occurs in the first vessel. Later optimization is performed and as the vessel size is held constant, the cooling agent just needs to cool fast enough. NaCl brine is the cheapest cooling agent. Even with NaCl brine, the maximum number of CSTR is limited to 3.

Subsequent cost optimization found 1 CSTR to be the cheapest with a summation of equipment cost and 2 years of operating cost to be $4,180,000. The second cheapest was 2 CSTR at $4,260,000, 3 or more CSTR cost over $4,390,000. The result was unexpected but is attributed to the fact that 1 CSTR model would not require a jacket, while 2 CSTR's has two reactors and a jacket or essentially 3 vessels. Although slightly more expensive, the 2 CSTR model was selected because: (1) reaction 1 was more complete (99.7% vs 100.0%), (2) it reduces the risk of poor mixing affecting the outlet composition - poor mixing would have to occur in two vessels rather than one, and (3) "groupings" are tighter allowing for erroneous products to be more easily identified and a smaller amount to be discarded. The CSTRs will both have a residence time of 23 minutes and contain 7,756 kg of material. Even though the vessel is small enough that glass lined steel can be used, to keep consistent with the batch process, Hastelloy was used. Both vessels will contain an agitator to ensure it is well mixed.

MSMPR

After the reaction vessels, the fluid will go through a series of mixed suspension–mixed product removal reactors, MSMPR's, to cool to 15 ^oC and crystallize the acetaminophen. Essentially the MSMPR will cool the fluid a certain amount and induce a known amount of crystallization depending on the temperature. Seeding is not necessary as after the initial startup, seeds will always be present in the vessel. The energy of cooling and necessary cooling agent needs to remove the energy in the same time frame was determined. The log mean temperature difference is between vessel temperature (not the 80 ^oC fluid) and cooling agent. With the overall heat transfer coefficient of the cooling agent, the jacket area and volume of the vessel are calculated. The MSMPR's are modeled as a vertical pressure vessel with an agitator and jacket. With an initial assumption of 3 MSMPR's, the cooling agent was optimized to be $CaCl_2$ brine, the higher cost of the agent was outweighed by the cost saved from smaller equipment sizes. Next the optimal number of MSMPR's was determined. Although 1 MSMPR was the cheapest at $10,400,000, 2 MSMPR at $10,700,000 was selected. This was because of (1) the relatively insignificant price difference, (2) one spare can be on hand for cheaper, and (3) "groupings" are tighter allowing for erroneous products to be more easily identified and a smaller amount to be discarded.

The first MSMPR cools the fluid from 80 °C to 42 °C, occupying 80.4 m^3 with a residence time of 3.97 hours. The second MSMPR further cools it to 15 °C utilizing 80.9 m^3 with a residence time of 4.00 hours.

Screw Press

As the nutsche filter is a batch process with clear delineation between the filtering and cake removal process, a continuous filter is utilized instead. A screw press was chosen because it's one of the few options available to continuously filter crystals out and available in SuperPro Designer. The slurry will be fed into the beginning of the screw at a rate of 337 kg/min and most of the liquid will be filtered out by the midpoint of the filter. An 8:2 acetic acid wash equal to half the mass of crystals, 33.0 kg/min, will commence around halfway in and finally a water wash, 33.0 kg/min, will commence after that. The exact positions of the washes will depend on how quickly the screw press can filter out the solids and the two washes are done to mimic the batch process. The drain will be split into two sections, the drain from the slurry with saturated acetaminophen and the drain from the washes which will contain negligible acetaminophen. This is again done to maximize the amount of acetaminophen recycled. The first drain will have 271 kg/min of fluid and 35.5%, or 96.3 kg/min, will be mixed with water and heated as discussed in the preheating heat exchanger section. The remaining will be pumped to the distillation column. The drainage from the washes will also be pumped to the distillation column to remove any acetaminophen dissolved.

The washes will be cooled to 15 °C to minimize loss of acetaminophen. The 8:2 acetic acid will come in at 76.8 °C and require 33.7 m^2 for a chilled water-cooling heat exchanger. While the standard temperature water will require a 21.4 m^2 heat exchanger for the same cooling agent. Both use double-pipe heat exchangers. NaCl Brine would reduce the cost, but as the cost is already relatively insignificant for this process, the optimization was not performed here.

Project consultants stated that such a method of washing the crystals is possible in a screw press, but SuperPro Designer does not have this option. As such, the streams simply start and end on the screw press where the desired location of the inputs and outputs are desired and are treated as if they are properly connected.

Preheating heat exchanger

Similar to the heat exchangers prior to the reaction, a heat exchanger will be used to heat the solvent up to 80 ^{o}C. The solvent will start at 30.2 ^{o}C due to the mixture of standard temperature acetic acid, 15 ^{o}C recycle, and 107 ^{o}C acetic acid and water from the distillation column. With a flow rate of 257.4 kg/min as determined in the mass balance and heating requirement to 80 ^{o}C, 5 atm steam is used, requiring 17.8 m^2 of area. With this small area, a double-pipe heat exchanger is used.

Similarly noted in the batch section, more thorough analysis is recommended to account for two more factors; the dissolving process of the cake releasing energy and fluid needing to maintain a temperature of 80 ^{o}C until it reaches the crystallization vessel. Such considerations will likely shift the necessary temperature down from 80 ^{o}C, but for simplicity and a conservative estimation, the solvent is heated to 80 ^{o}C.

Dissolver

The dissolving vessel will consist of a vertical pressure vessel with an agitator to ensure the contents are well mixed. As mentioned in the batch dissolver, acetaminophen seems to dissolve at a relatively reasonable rate. To be conservative, a residence time of 30 minutes was assumed and the acetaminophen cake is transferred from the screw press using a screw feeder with the solvent transferred from the preheating heat exchanger. With a residence time of 30 minutes, the vessel needs to handle 9,536 kg of material. For optimization, the residence time and thus size of the vessel can likely be reduced.

Granular Activated Carbon

After dissolving the acetaminophen, the fluid is fed through a column filled with granular activated carbon to remove any impurities from the stream. Again, as mentioned in batch, due to the paucity of isotherm data, very conservative estimations of activated carbon needs are priced here and kept consistent with batch.

With a flow rate of 317.9 kg/min, or 8.60 ft3/min, and the expected flow rate of 1 ft/min within the column, 8.60 ft2 cross sectional area is needed. A calculation error occurred here and the diameter was calculated to be 5.87 ft instead of the actual 3.31 ft diameter. With the erroneous diameter, height was determined to be 13.73 ft, two times the diameter plus two feet, and volume 371 ft3. Utilizing the 125 lb/ft3 density, 85% full, and 74% packing density of spheres, 29,172 kg of activated carbon is loaded into the tank. Using the same assumption as in batch, 1% of the mass flowing through it is used up of the activated carbon, so the column lasts 2.9 days before the activated carbon needs to be replaced. Two columns will be used such that one can always be in use while the other is unloaded and loaded with new activated carbon.

With the corrected diameter, the column would be approximately $300,000 cheaper and the column would have to be switched every 0.58 days instead. Note that a time of one day and a slightly larger vessel may be desired to keep the switching time consistent.

MSMPR

The MSMPR will essentially operate in the same manner as the first set, where the fluid is cooled to 15 ^{o}C and the acetaminophen crystallizes out. Due to the loss of acetaminophen, the flow rates are 19.4 kg/min less than the MSMPR used in the first crystallization process, at 317.9 kg/min. As the mass is still within the same magnitude, the optimization for the MSMPR was assumed to hold true here as well. As such with 2 MSMPR and $CaCl_2$ brine cooling agent, the first MSMPR cools from 80 ^oC to 42 ^oC occupying 75.6 m^3 with a residence time of 3.73 hours and the second MSMPR cools further to 15 ^oC occupying 76.0 m^3 with a residence time of 3.76 hours.

Screw press

The screw press will operate in the same manner as the first one. The slurry will enter at the beginning of the screw and most of the liquid will fall out by around the middle. That liquid is saturated with acetaminophen and 75%, 195.1 kg/min, will be recycled to the solvent preheating heat exchanger, while the remaining 25%, 59.4 kg/min, go to the distillation column. The 8:2 wash, 31.7 kg/min, will enter about halfway and finally the water wash, 31.7 kg/min, will enter near the end as the final wash. The drainage from the washes will be pumped to the distillation column.

The wash liquid will need to be cooled to 15 ^oC and unoptimized chilled water is utilized because optimization of this process unit has relatively insignificant effect on cost. The 8:2 ratio acetic acid to water is cooled from 76.8 ^oC, thus requiring 32.3 m^2 and the standard temperature water wash requires 20.6 m^2.

It may be more economical to combine the wash streams with their respective streams for the first screw press, as costs will be saved on the pumps and heat exchanger. But the unknown placement of equipment units may make this difficult, so they are modeled to be separate here.

Fluid drying bed

As the screw press is unable to fully dry the acetaminophen cake, unlike the nutsche filter, a fluid drying bed is necessary to dry the acetaminophen. The wet cake is transferred into the fluid drying bed with a screw feeder. Assuming the cake is still fairly wet, 50% of the mass is composed of liquid that can be dried off, 4,095.92 kg/hr (108% the mass of cake). With a drying rate of 3.00 lb/hrft3[32], a volume of 3,009 ft^3 is necessary. In a vessel with 6 times the height than diameter, the surface area necessary is 1,398 ft^2. The dried acetaminophen is transferred out to an off-site storage tank using a screw feeder.

As a significant mass of fluid will need to be dried off here, the fluid coming from the drainage of the screw press is inaccurate and future models can better address this with improved information on the wetness of the cake.

Distillation

A simple continuous distillation process, modeled with a vertical pressure vessel and two heat exchangers, will be performed to separate as much of the acetic acid and water from the waste as possible to be reused or sold. Adding up all the streams, purge from recycles, and washes, it is composed of 9.9 kg/min of acetaminophen, 236 kg/min of acetic acid, and 124 kg/min of water. To ensure the bottoms flow well, the g acetaminophen/kg solvent is not allowed to exceed 200, thus forcing the bottoms solvent flow rate to be 49.4 kg/min with the remaining 310 kg/min as the distillate. Utilizing the T-xy diagram in Section 9, the temperature was determined to be 107 ^oC with mass fractions of 0.76 acetic acid in the bottoms, ignoring the acetaminophen, and 0.64 acetic acid in the distillate. The heating required will involve heating all 369 kg/min of inputs from 15 ^oC to 107 ^oC and evaporate the distillate — 198 kg/min of acetic acid and 112 kg/min of water. Using 5 atm steam, 336 m^2 of area is required. For the condensing, the fluid will only be transformed from the gaseous state to the liquid state and left at 107 ^oC. With NaCl Brine, 630 m^2 of area is required. As recommended by consultants, half the volume of the vertical pressure will contain ten minutes of feed, 260 m^3 of volume is necessary.

70.4 kg/min of the distillate will be combined with 56.7 kg/min of acetic acid to form an 8:2 ratio of acetic acid to water solution which will be used for the solvent for the dissolver and washes. As the flow is continuous and timing is not a consideration, a vessel to control timing like in the batch process is unnecessary. The remaining 240 kg/min of distillate will be collected in an off-site storage tank to be sold. The bottom product, waste, will be transferred to an off-site storage tank.

Off-site storage

Same as in the batch process, three off-site storage tanks will be necessary — for acetaminophen, acetic acid plus water distillate, and bottoms waste. A two-week storage capacity is necessary here as well. With continuous operation over that entire time period, 1,279,000 kg of acetaminophen, 4,830,000 kg of acetic acid plus water distillate, and 1,195,000 kg of bottoms waste will need to be stored. Again, as the continuous process operates for more time in a year and does not require active seeding, the production over two weeks will be less than the batch process. With such a volume, cone-roof storage tanks are used. The distillate and bottoms will both enter the tank at 107 ^{o}C and will naturally cool. Consideration was given to heating the tanks to prevent freezing, but with a location of India, the tanks will not get cold enough for the fluid within to freeze.

Figure 11.5: Continuous PFD

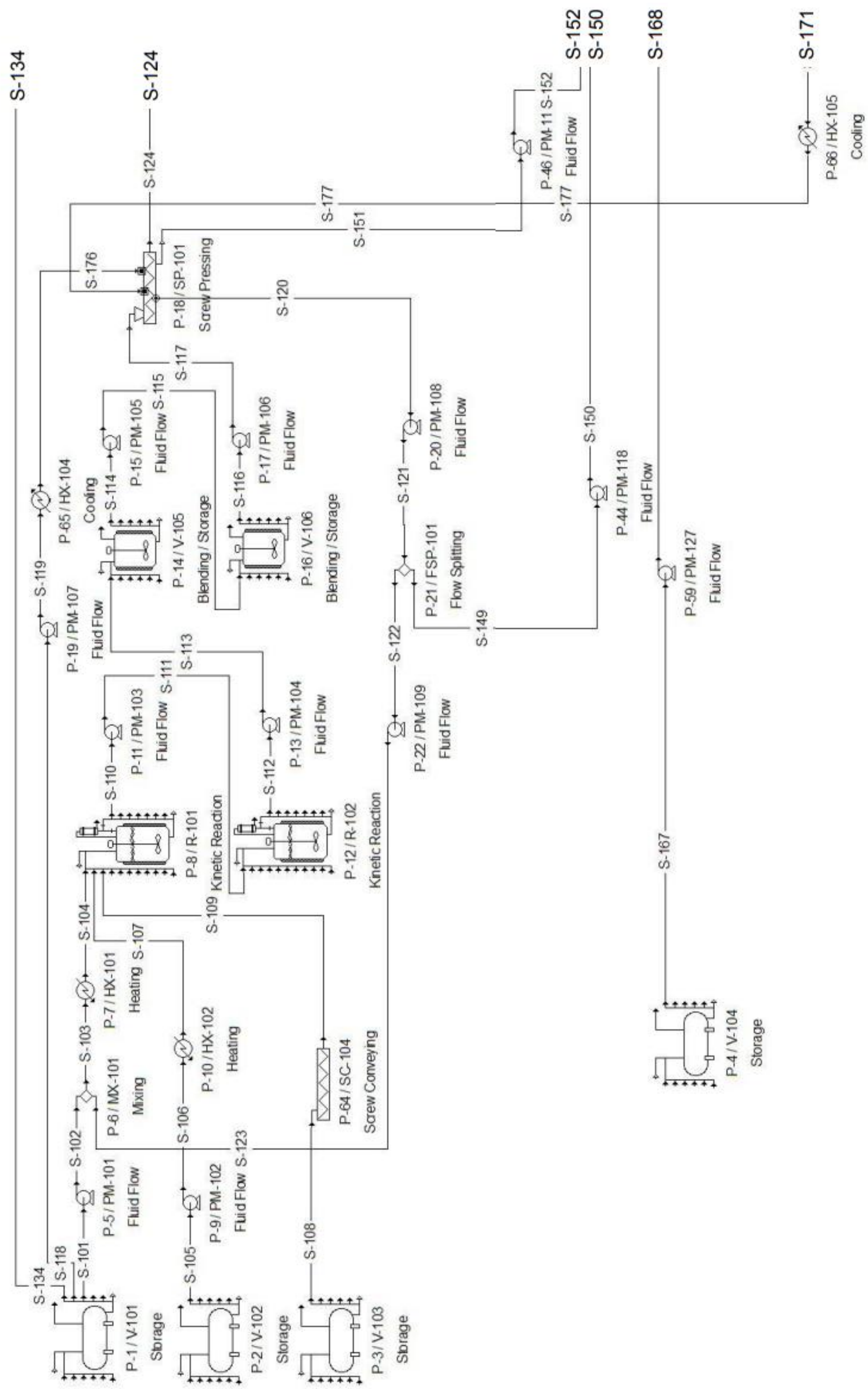


Figure 11.5: Continuous PFD Cont.

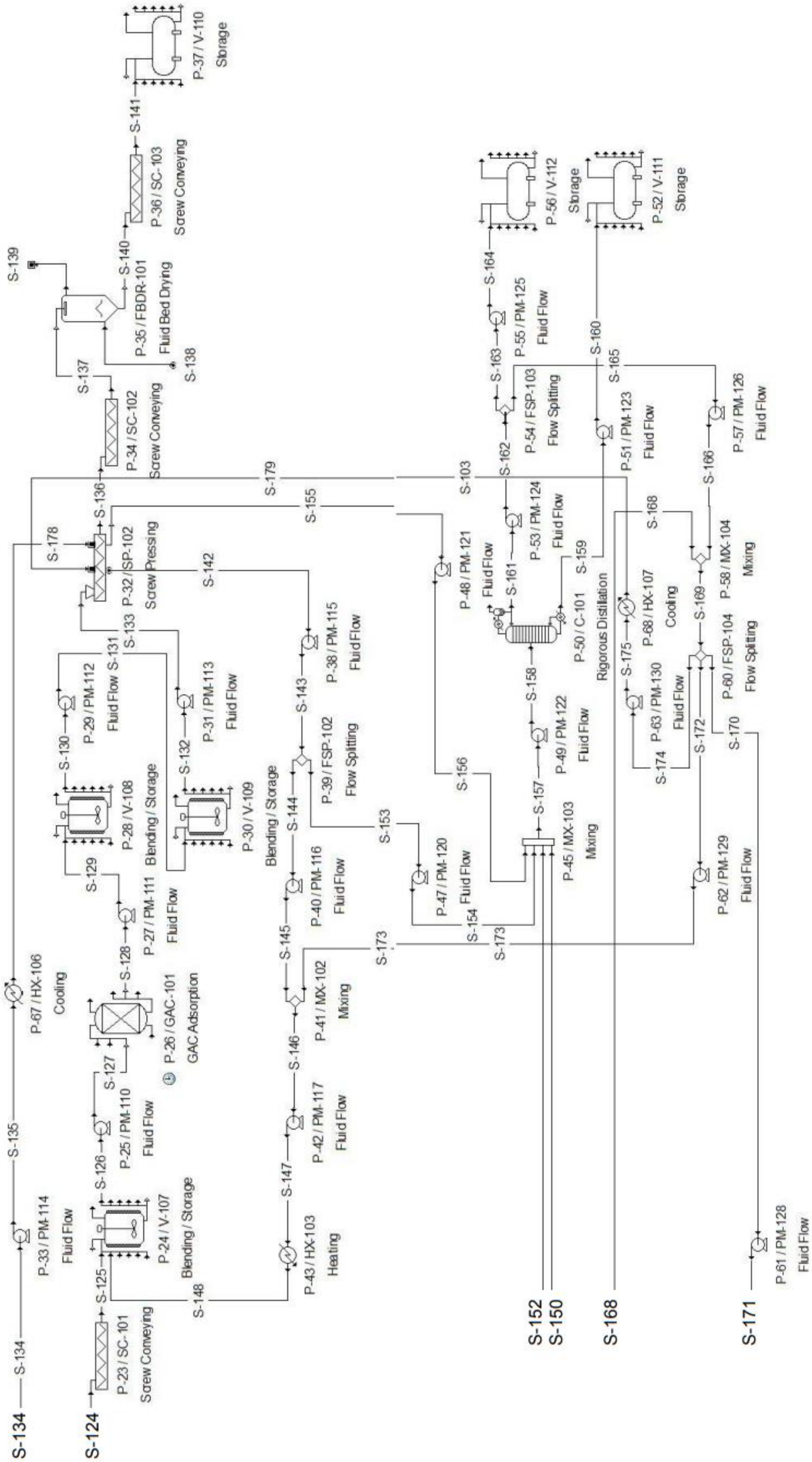


Figure 11.6: Continuous Stream Properties

		S-101	S-102	S-103	S-104	S-105	S-106	S-107	S-108	S-109
State of Matter		L	L	L	L	L	L	L	S	S
Mass	kg/min	49.2	49.2	145.6	145.6	138.7	138.7	138.7	52.9	52.9
Acetaminophen	kg/min			4.0	4.0					
Acetic Acid	kg/min			73.9	73.9					
Water	kg/min	49.2	49.2	67.7	67.7					
P-aminophenol	kg/min								53.0	53.0
Acetic Anhydride	kg/min					138.7	138.7	138.7		
Mol	kmol/min	2.733	2.733	5.016	5.016	1.359	1.359	1.359	0.485	0.485
Temperature	C	25	25	19.7	53.7	25	25	53.7	25	25
Density	kg/m^3	1000	1000	1044	1044	1080	1080	1080	1130	1130
Volumetric flow	m^3/min	0.0492	0.0492	0.1394	0.1394	0.1284	0.1284	0.1284	0.0468	0.0468

	S-110	S-111	S-112	S-113	S-114	S-115	S-116	S-117	S-118	S-119
State of Matter	L	L	L	L	L	L	L	L	L	L
Mass	337.2	337.2	337.2	337.2	337.2	337.2	337.2	337.2	33.0	33.0
Acetaminophen	75.8	75.8	77.3	77.3	77.3	77.3	77.3	77.3		
Acetic Acid	189.4	189.4	207.9	207.9	207.9	207.9	207.9	207.9		
Water	54.7	54.7	52.0	52.0	52.0	52.0	52.0	52.0	33.0	33.0
P-aminophenol	1.1	1.1								
Acetic Anhydride	16.3	16.3								
Mol	6.859	6.859	6.859	6.859	6.859	6.859	6.859	6.859	1.835	1.835
Temperature	80	80	80	80	42	42	15	15	25	25
Density	1330	1330	1328	1328	1328	1328	1328	1328	1000	1000
Volumetric flow	0.2536	0.2536	0.2538	0.2538	0.2538	0.2538	0.2538	0.2538	0.0330	0.0330

Figure 11.6: Continuous Stream Properties Continued

	S-120	S-121	S-122	S-123	S-124	S-125	S-126	S-127	S-128	S-129
State of Matter	L	L	L	L	S	S	L	L	L	L
Mass	271.1	271.1	96.3	96.3	66.1	66.1	323.5	323.5	323.5	323.5
Acetaminophen	11.2	11.2	4.0	4.0	66.1	66.1	74.1	74.1	74.1	74.1
Acetic Acid	207.9	207.9	73.9	73.9			199.5	199.5	199.5	199.5
Water	52.0	52.0	18.5	18.5			49.9	49.9	49.9	49.9
Mol	6.422	6.422	2.282	2.282	0.437	0.437	6.581	6.581	6.581	6.581
Temperature	15	15	15	15	15	15	80	80	80	80
Density	1068	1068	1068	1068	1260	1260	1328	1328	1328	1328
Volumetric flow	0.25384	0.25384	0.09022	0.09022	0.05246	0.05246	0.24355	0.24355	0.24355	0.24355
	S-130	S-131	S-132	S-133	S-134	S-135	S-136	S-137	S-140	S-141
State of Matter	L	L	L	L	L	L	S	S	L	L
Mass	323.5	323.5	323.5	323.5	31.7	31.7	63.4	63.4	63.4	63.4
Acetaminophen	74.1	74.1	74.1	74.1			63.4	63.4	63.4	63.4
Acetic Acid	199.5	199.5	199.5	199.5						
Water	49.9	49.9	49.9	49.9	31.7	31.7				
Mol	6.581	6.581	6.581	6.581	1.760	1.760	0.420	0.420	0.420	0.420
Temperature	42	42	15	15	25	25	15	15	25	25
Density	1328	1328	1328	1328	1000	1000	1260	1260	1260	1260
Volumetric flow	0.24355	0.24355	0.24355	0.24355	0.03171	0.03171	0.05033	0.05033	0.05033	0.05033
	S-142	S-143	S-144	S-145	S-146	S-147	S-148	S-149	S-150	S-151
State of Matter	L	L	L	L	L	L	L	L	L	L
Mass	260.1	260.1	195.1	195.1	257.4	257.4	257.4	174.7	174.7	66.1
Acetaminophen	10.7	10.7	8.0	8.0	8.0	8.0	8.0	7.2	7.2	
Acetic Acid	199.5	199.5	149.6	149.6	199.5	199.5	199.5	134.0	134.0	26.4
Water	49.9	49.9	37.4	37.4	49.9	49.9	49.9	33.5	33.5	39.7
Mol	6.161	6.161	4.621	4.621	6.144	6.144	6.144	4.139	4.139	2.642
Temperature	15	15	15	15	30.2	30.2	80	15	15	15
Density	1068	1068	1068	1068	1057	1057	1057	1068	1068	1012
Volumetric flow	0.24355	0.24355	0.18266	0.18266	0.24355	0.24355	0.24355	0.16362	0.16362	0.06533

Figure 11.6: Continuous Stream Properties Continued

	S-152	S-153	S-154	S-155	S-156	S-157	S-158	S-159	S-160	S-161
State of Matter	L	L	L	L	L	L	L	L	L	L
Mass	66.1	65.0	65.0	63.4	63.4	369.3	369.3	59.3	59.3	310.0
Acetaminophen		2.7	2.7			9.9	9.9	9.9	9.9	
Acetic Acid	26.4	49.9	49.9	25.4	25.4	235.7	235.7	37.6	37.6	198.1
Water	39.7	12.5	12.5	38.1	38.1	123.7	123.7	11.8	11.8	111.9
Mol	2.642	1.540	1.540	2.535	2.535	10.856	10.856	1.345	1.345	9.511
Temperature	15	15	15	15	15	15	15	107	107	107
Density	1012	1068	1068	1012	1012	1048	1048	1227	1227	1019
Volumetric flow	0.06533	0.06089	0.06089	0.06268	0.06268	0.35252	0.35252	0.04830	0.04830	0.30422

	S-162	S-163	S-164	S-165	S-166	S-167	S-168	S-169	S-170
State of Matter	L	L	L	L	L	L	L	L	L
Mass	310.0	239.6	239.6	70.4	70.4	56.7	56.7	127.1	33.0
Acetaminophen									
Acetic Acid	198.1	153.1	153.1	45.0	45.0	56.7	56.7	101.7	26.4
Water	111.9	86.5	86.5	25.4	25.4			25.4	6.6
Mol	9.511	7.351	7.351	2.160	2.160	0.944	0.944	3.104	0.807
Temperature	107	107	107	107	107	25	25	76.8	76.8
Density	1019	1019	1019	1019	1019	1030	1030	1024	1024
Volumetric flow	0.30422	0.23513	0.23513	0.06909	0.06909	0.05505	0.05505	0.12414	0.03228

	S-171	S-172	S-173	S-174	S-175	S-176	S-177	S-178	S-179
State of Matter	L	L	L	L	L	L	L	L	L
Mass	33.0	62.3	62.3	31.7	31.7	33.0	33.0	31.7	31.7
Acetaminophen									
Acetic Acid	26.4	49.9	49.9	25.4	25.4		26.4		25.4
Water	6.6	12.5	12.5	6.3	6.3	33.0	6.6	31.7	6.3
Mol	0.807	1.523	1.523	0.774	0.774	1.835	0.807	1.760	0.774
Temperature	76.8	76.8	76.8	76.8	76.8	15	15	15	15
Density	1024	1024	1024	1024	1024	1000	1024	1000	1024
Volumetric flow	0.03228	0.06089	0.06089	0.03097	0.03097	0.03305	0.03228	0.03171	0.03097

Section 12: Energy Balance and Utility Requirements

There are five main domains of energy and utility for both plants: cooling agents, heating agents, granular activated carbon, electricity, and waste treatment.

12.1: Cooling Agents

Cooling agents are used on four components of the process: the reaction and crystallization, the recrystallization, the filter washes, and the distillation column condensers. As determined in the Section 9, based on the temperature change, heat capacity, and cost, the energy removed per dollar of cooling agent can be quantified to provide a standardized comparison between options. The cooling agents used are practically identical between the batch and continuous process: $CaCl_2$ brine for both crystallizations, NaCl brine for the distillation condensation, and chilled water for the washes (not optimized). The only difference is that the batch reactor used $CaCl_2$ brine to cool the reactor at a faster rate while the continuous used NaCl brine because the volume was controlled by the residence time and NaCl brine could cool at an adequate rate.

For the batch process utilities, the reaction and first crystallization costs $315,000/year, the recrystallization $283,000/year, washes $129,000/year, and distillation $1,603,000/year for a total of $2,331,000/year. With the same breakdown, the continuous utilities cost $292,000/year for the reaction and crystallization, $267,000/year for recrystallization, $121,000/year for washes, and $1,526,000/year for distillation for a total of $2,206,000/year. As can be seen, the cost for continuous is slightly lower on all aspects and this is mainly attributed to the way seeding is handled.

12.2: Heating Agents

Heating agents can be broken down between three processes: reactor, dissolver, and heater/evaporator for distillation column. As all processes demand a temperature less than 110 ^{o}C, 5 atm steam at 152 ^{o}C was determined to be the most efficient heating agent for all processes. In an identical method to the cooling agents, the cost per joule of heating was determined to be 176 MJ/$ for 5 atm steam.

For the batch process utilities, the reactor preheaters cost $47,000/year, the dissolver preheater $92,000/year, and the distillation $1,537,000/year for a total of $1,676,000/year. While for the continuous process utilities, the reactor preheaters cost $61,000/year, the dissolver preheater $89,000/year, and the distillation $1,464,000 for a total of $1,614,000/year. Much like the cooling agents, the cost is typically slightly lower in the continuous process due to the seeding process. The batch reactor preheater utility is slightly lower than continuous, this may appear unexpected, but the batch preheater only heats to 46 ^{o}C while the continuous heats to 53.7 ^{o}C.

12.3: Granular Activated Carbon

The granular activated carbon will be used to remove impurities prior to recrystallization. An assumption was made that the activated carbon will be used up at a rate equal to 1% of the mass of the material passing through it. Sized as a 2:1 length to diameter cylinder with a throughput of 1ft^3/min - a conservative estimate according to Seider Textbook, the column needed to be 371 ft^3. The unit was priced as Hastelloy as well to be a $560,000 process unit. Following empirical analysis on the activated carbon properties, more refined calculations for sizing and consumption can be made. It is important to recognize that the same assumptions for batch and continuous were made for this unit.

12.4: Electricity

Electricity will be used in the motors of the agitators, pumps, and screws.

The agitators were corrected to have an efficiency of 95% and the horsepower for the vertical pressure columns was 1.5hp/1000 gal. The method of determining volumes was described above and thus quickly, kilo-watt needs could be found. For batch, the agitators were active for 5226 hours and the cost of electricity was given as $0.07/kw-hr. The continuous agitators were priced and sized the same way; however, their run time was 7884 hours. The continuous agitators consumed more electricity at a cost of $67,000/year compared to batch's $31,000/year. This is mainly attributed to the large agitators required for the 4 MSMPR.

Centrifugal pumps and electric motors were used to pump the liquids. The power consumption of the motors was calculated based on the flow rate and density, which are known, and the head was assumed to be 100 ft. There are two more factors, the fractional efficiency of the pump and of the electric motor, but these are a function of the flow rate and pump brake horsepower, both of which can be determined using the same variables. Assuming another 95% efficiency and utilizing the amount of time each motor will be in a year, the kWhr/year can be calculated. Multiplied by electricity cost $0.07/kWhr gives the electrical cost a year. It comes out to $76,000 a year for a batch and $65,000 for continuous. A big factor towards the cost difference is that the staggered equipment in batch will each require a pump, increasing the total number of pumps, and the shortened time period of use, say 10 minutes of every 2-hour cycle time, also increases costs. If the same pump can be used for multiple streams, it may be possible to reduce this cost. .

For the screw feeders, the solid transfer processes, and the electric motors associated with each both, the horsepower is determined based on the flow rate and length, assumed to be 100 ft. The horsepower, length of time in use, 95% efficiency, and cost of electricity are factored in to give the cost of electricity a year. Batch comes out to $19,000/year and continues to $5,000/year. Like the pumps, the shortened time the feeders are active makes them less efficient.

12.5: Waste Treatment

The waste is composed of the components from the bottoms stream of the distillation tower. It will contain acetaminophen, acetic acid, water, and impurities and be collected in an off-site horizontal tank. Initially, incineration, $0.45/lb, was planned for burning the stream, but consultants advised burning in a cement kiln as the stream is composed of relatively high BTU material, reducing the cost to $0.09/lb. As the batch process generates 8,133 kg/batch at 3,504 batches a year, the cost comes to $5,654,000/year. For the continuous, 59.28 kg/min at 328.5 days comes out to $5,564,000/year. Both costs are very similar.

One aspect not accounted for is that the stream involves large amounts of acetic acid which may need to be neutralized first and as such, there may be an additional cost to purchasing and burning the neutralizing agent. However, the mass and composition of both the batch and continuous process are relatively similar, this will have negligible impact on the cost difference of the two.

The utility cost of the batch process totals $9,850,480 and the continuous process totals $9,572,574. As expected, the batch process is slightly more expensive, this can mainly be attributed to the seeding method requiring more material.

Section 13: Equipment List and Unit Descriptions

13.1: Batch Process

Off-site storage

The off-site storage tanks store the material prior to their use in the process. They are numbered V-101, V-102, V-103, V-104 for the water, acetic anhydride, p-aminophenol, and acetic acid storage respectively. Cone-roof storage tanks are used, and pumps or screw feeders are connected to transfer liquid or solid material out respectively. The water and p-aminophenol storages were constructed of carbon steel while the acetic acid storage used polypropylene lined steel. Using Chapter 16 of Seider textbook, shown in A.7, V-101 costs $1,000,000, V-102 $1,772,000, V-103 $863,000 for a total of $3,635,000.

Reactor preheating

Double-pipe heat exchangers, HX-101 and HX-102, are used to heat the reactants and vertical pressure vessels with agitators, V-105 and V-106, hold the heated liquids prior to pumping it into the reactor. HX-101 and V-105 receive water, acetic acid, and acetaminophen from the water storage tank, V-101, and the recycle storage, V-108, while HX-102 and V-106 receive acetic anhydride from the acetic anhydride storage tank, V-102. The storages are priced as Hastelloy, and heat exchangers have a stainless steel interior and carbon steel exterior. Using the Seider textbook, HX-101 costs $10,000, V-105 $1,927,000, HX-102 $9,000, and V-106 $1,922,000. Calculations shown in A.7 for heat exchangers and vertical pressure vessels.

Reactor

The reactor vessel, R-101, is a jacketed vertical pressure vessel with an agitator. This unit will receive the material from V-105 and V-106 and contain the reaction, subsequently cooling the fluid to 15 C and allowing for crystallization. All pieces of the equipment are constructed of Hastelloy. Each reactor vessel will cost $3,754,000, and with staggering, 4 are required and an additional spare was priced.

Storage Vessel

A vertical pressure vessel with an agitator, V-107, receives the cooled fluid from the reactor vessel, R-101, and controls the rate the slurry is fed into the nutsche filter. This will be constructed of Hastelloy and cost $1,890,000.

Nutsche filter

The agitated nutsche filter, NFD-101, receives a slurry from V-107 and separates the acetaminophen crystals from the slurry. The filter will be priced as a Hastelloy rotary-drum vacuum and each one will cost $1,634,000 as priced in A.7. Two are staggered with one spare. Two double-pipe heat exchangers will also be associated with this process to cool the washes down to 15 C to be used. HX-105 will receive fluid from V-119 and cost $15,000, while HX-104 will receive fluid from the water storage tank, V-101, and cost $15,000. The heat exchanger is priced with a stainless-steel inner pipe and outer pipe of carbon steel.

Recycle 1

A Hastelloy vertical pressure vessel with an agitator, V-108, will receive the drainage from the nutsche filter that is saturated with acetaminophen. This unit will recycle a portion of its liquid back to the reactor preheater. It costs $1,134,000.

Solvent Preheater

A double-pipe heat exchanger, HX-103, and vertical pressure vessel with agitator, V-111, will be used to heat and store the solvent used for the recrystallization process. The agitator is priced as Hastelloy, and all following double pipe heat exchangers are priced with a stainless-steel interior and carbon steel exterior. The heat exchanger receives material from V-115 and V-119 and heats and delivers it to the vessel. The heat exchanger costs $12,000, while the vessel costs $1,899,000.

Dissolver

A Hastelloy vertical pressure vessel with an agitator, V-110, will dissolve the acetaminophen for the recrystallization process. The fluid from the solvent preheater, V-111, will be pumped in and the cake from the nutsche filter will be screw fed into this vessel and the agitation will aid in the dissolution of the cake. This vessel will cost $1,891,000.

Granular Activated Carbon

A Hastelloy vertical pressure vessel with an agitator, GAC-101, will be filled with granular activated carbon. The fluid from the dissolver, V-110, will be pumped through this such that impurities are removed by the granular activated carbon. The vessel costs $2,105,000, two will be necessary as the column will need to be switched out when replacing the carbon.

Recrystallizer

A Hastelloy autoclave, V-112, will be used to recrystallize the acetaminophen out of the solution by cooling the temperature down to 15 ^{o}C. The autoclave formulation includes the jacket and agitator necessary for the cooling process. Each equipment will cost $1,076,000 and four will need to be staggered to reach the desired batch time and a spare is also prepared.

Storage Vessel

A vertical pressure vessel with an agitator, V-113, receives the cooled fluid from the recrystallizer, V-112, and controls the rate the slurry is fed into the nutsche filter. This will be constructed of Hastelloy at a cost of $2,040,000

Nutsche Filter 2

The agitated nutsche filter, NFD-102, receives a slurry from V-113 and separates the acetaminophen crystals from the slurry. The filter will be made from Hastelloy and priced as rotary-drum vacuums. Each one will cost $1,563,000; six are staggered with one spare. These are very close in size to the Nutsche in P-19 so the spare can go there as well.

Two double-pipe heat exchangers will also be associated with this process to cool the washes down to 15 ^{o}C to be used. HX-107 will receive fluid from V-119 and cost $15,000, while HX-106 will receive fluid from the water storage tank, V-101, and cost $15,000. It may be possible to combine these with the heat exchangers HX-105 and HX-104 respectively, but with the unknown layout of the plant they were left separate to be conservative.

Distillation

The feed into the distillation column will be collected in V-116, a Hastelloy vertical pressure column, and V-108 and V-115 discussed in the recycle 1 and recycle 2 sections respectively.

The distillation column will be composed of a vertical pressure vessel with a height three times that of the diameter and two fixed head heat exchangers. Operating at room pressure, the feed will get heated to 107 ^{o}C and be separated in a distillate and bottoms component. The vessel will cost $2,538,000 with one spare, the heating and cooling heat exchangers will cost $159,000 and $285,000 respectively.

The bottoms and part of the distillate will be pumped to off-site storage tanks V-117 and V-118 respectively, A portion of the distillate will go to a Hastelloy vertical pressure tank, V-119, where it's mixed with acetic acid from V-104 to form acetic acid and water in an 8:2 ratio. This vessel, V-119 will cost $1,229,000

Off-site Storage

Cone-roof storage tanks will be used to store the products, V-114 for acetaminophen, V-118 for the acetic acid and water solution, and V-117 for waste. These will hold up to 2 weeks' worth of product so that the plant can keep producing. Polypropylene lined steel V-118 will cost $2,318,000 and V-117 will cost $1,016,000.

Pumps, Mixers, and Splitters

There will be a total of 47 pumps and electric motors throughout the system to transfer fluids between different process units, this number is bolstered by the fact that staggered units will need their own pumps. All the pumps are 1 stage vertical centrifugal pumps operating at 3,600 rpm.

Every pump is constructed of Hastelloy except the ones only in contact with water, PM-101, PM-107, and PM-115, are carbon steel. Open, drip-proof enclosure electric motors at 3,600 rpm are paired with each one. The pumps will all operate at a less than 700 gal/min and ones below 50 gal/min are rounded up to 50 gal/min as the formula used does not accurately estimate below that range. Each pump and motor set will range between $20,000 to $136,000 for a sum total of $4,541,000.

Mixers and splitters although shown in the process flow diagram will not be priced, the pipe head priced into the pump cost is assumed to cover these as well.

Screw Feeders

Five screw feeders and electric motors will be used throughout the plant to transport solids. The screw feeders are priced as Hastelloy and the same type of motor as the pumps are used, open, drip-proof enclosure electric motors at 3,600 rpm. They range in price from $72,000 to $99,000 for a total of $432,000.

13.2: Continuous Process

Off-site storage

Much like the batch process, four cone-roof storage tanks are used to store material prior to their use. Water storage, V-101, and p-aminophenol storage, V-103, will be made of carbon steel and cost $215,000 and $187,000 respectively. Acetic anhydride storage, V-102, will be made of polypropylene lined steel and cost $595,000. Note this missing cost is on both the continuous and batch process.

Reactor preheating

Two double-pipe heat exchangers, HX-101 and HX-102, are used to heat the reactants prior to the reactor vessel. R-101, a heat exchanger heats a combination of water, acetic acid, and acetaminophen coming from the water tank, V-101, and the drainage of the first screw press filter, SP-101. HX-102, another heat exchanger heats acetic anhydride from V-102. HX-101 costs $10,000 and HX-102 costs $8,000.

Reactor

A series of two Hastelloy vertical pressure vessels, R-101 and R-102, will act as a CSTR system to allow the reaction to take place. R-101 will receive material from the two heat exchangers, HX-101 and HX-102, as well as the p-aminophenol from its storage, V-103. While R-102 will receive the materials from R-101, this is done to ensure a more complete reaction is performed. Both vessels will contain an agitator and a jacket. R-101 will cost $2,054,000 and R-102 will cost $2,188,000. A spare will be prepared for both vessels.

Crystallizers

Two Hastelloy vertical pressure vessels, V-105 and V-106, are connected in series and will receive the material from the second CSTR reactor, R-102. The fluid will be cooled in the vessels and with crystals already present, the desired crystallization will occur. Both will include a jacket and agitator to ensure efficient cooling. They will cost $5,421,000 and $5,436,000 respectively and future optimization should bring them to be the same size, so they are interchangeable. A spare is priced for the more expensive one such that it can take the place of either if necessary.

Screw Press Filter

The Hastelloy screw press filter, SP-101, will receive the slurry from V-106 and separate the liquid from the crystals. Two washes will be performed mid-way into the filter to wash the crystals. It will cost $2,222,000 and a spare will be prepared.

Two double-pipe heat exchangers will also be associated with this process to cool the washes down to 15 ^{o}C to be used. HX-105 will receive fluid from a mix of acetic acid storage, V-104, and distillation, C-101, and cost $12,000, while HX-104 will receive fluid from the water storage tank, V-101, and cost $12,000.

The drainage from the filter will be split into two streams. The first part, from the slurry and saturated with acetaminophen, will be recycled as mentioned in the reactor preheater, HX-101, and excess will be sent to distillation, C-101. While the second part, composed of the washes, will be sent directly to distillation, C-101.

Solvent Preheater

A Hastelloy double-pipe heat exchanger, HX-103 will be used to heat the solvent used for the recrystallization process. The heat exchanger receives material from SP-102, C-101 and V-104 and delivers it to the dissolving vessel, V-107. It costs $11,000.

Dissolver

A Hastelloy vertical pressure vessel with an agitator, V-107, will re-dissolve the acetaminophen for the recrystallization process. The fluid from the solvent preheater, HX-103, will be pumped in and the cake from the screw press filter will be screw fed into this vessel and the agitation will aid in the dissolution of the cake. This vessel will cost $562,000.

Granular Activated Carbon

A Hastelloy vertical pressure vessel with an agitator, GAC-101, will be filled with granular activated carbon. The fluid from the dissolver, V-107, will be pumped through this such that impurities are removed by the granular activated carbon. The vessel costs $86,000, two will be necessary as the column will need to be switched out when replacing the carbon.

Recrystallizers

Two Hastelloy vertical pressure vessels, V-108 and V-109, are connected in series and will receive the material from the second granular activated carbon column, GAC-101. The fluid will be cooled in the vessels and with crystals already in it, the desired crystallization will occur. Both will include a jacket and agitator to ensure efficient cooling. They will cost $5,275,000 and $5,288,000 respectively and future optimization should bring them to be the same size, so they are interchangeable. A spare is priced for the more expensive one such that it can take the place of either if necessary.

Screw Press Filter 2

The Hastelloy screw press filter, SP-102, will receive the slurry from V-109 and separate the liquid from the crystals. Two washes will be performed mid-way into the filter to wash the crystals. It will cost $1,333,000 and a spare will be prepared. The cost of procurement was obtained from a manufacturer.

Two double-pipe heat exchangers will also be associated with this process to cool the washes down to 15 ^{o}C to be used. HX-107 will receive fluid from a mix of acetic acid storage, V-104, and distillation, C-101, and cost $11,000, while HX-106 will receive fluid from the water storage tank, P-101, and cost $12,000.

The drainage from the filter will be split into two streams. The first part, from the slurry and saturated with acetaminophen, will be recycled as mentioned in the dissolver preheater, HX-103, and excess will be sent to distillation, C-101. While the second part, composed of the washes, will be sent directly to distillation, C-101.

Fluid Drying Bed

The wet crystals from the second screw press, SP-102, will go to the fluid drying bed, FBDR-101, to be dried out. The fluid bed will be modeled as an indirect heat rotary dryer constructed of stainless steel. A spare will be prepared and each one will cost $1,832,000. After this fluid bed, the crystals will be transferred to an off-site storage tank for acetaminophen.

Distillation

The distillation column will be composed of a vertical pressure vessel with a height three times that of the diameter and two fixed head heat exchangers. As enumerated in previous parts, the feed will be composed of the excess recycles and washes of the screw press filters, SC-101 and SC-102. Operating at room pressure, the feed will get heated to 107 ^{o}C and be separated in a distillate and bottoms component. All components will be composed of Hastelloy. The vessel will cost $856,000 with one spare, the heating and cooling heat exchangers will cost $82,000 and $131,000 respectively.

The bottoms and part of the distillate will get pumped to off-site storage tanks V-111 and V-112 respectively. A portion of the distillate will get mixed in with acetic acid from P-4 and sent to the screw press filters or the solvent dissolver.

Off-site Storage

Cone-roof storage tanks will be used to store the products, V-110 for acetaminophen, V-112 for the acetic acid and water solution, and V-111 for waste. These will hold up to 2 weeks' worth of product. Polypropylene lined steel V-112 will cost $2,137,000, and polypropylene lined steel V-111 will cost $949,000.

Pumps, Mixers, and Splitters

There will be a total of 35 pumps and electric motors throughout the system to transfer fluids between different process units. All the pumps are 1 stage vertical centrifugal pumps operating at 3,600 rpm. Every pump is constructed of Hastelloy except the ones only in contact with water, PM-101, PM-107, and PM-114, are carbon steel. Open, drip-proof enclosure electric motors at 3,600 rpm are paired with each one. All the pumps will operate under 100 gal/min with the majority also below 50 gal/min. As the formula is only accurate to 50 gal/min and the price actually increases below that, every pump is rounded up to 50 gal/min and the price of pumps and motors is going to be decently overestimated. Each pump and motor set will range between $22,000 to $91,000 for a sum total of $3,109,000.

Mixers and splitters although shown in our process flow diagram will not be priced, the pipe head priced into the pump cost is assumed to cover these as well.

Screw Feeders

Four screw feeders and electric motors will be used throughout the plant to transport solids. The screw feeders are priced as Hastelloy and the same type of motor as the pumps are used, open, drip-proof enclosure electric motors at 3,600 rpm. They range in price from $65,000 to $66,000 for a total of $264,000.

Section 14: Specification Sheets

14.1: Batch Process

Reaction Preheater 1			
	Item		Heat Exchanger
	Item No.		HX-101
	No. Required		1
Function:	Heats water, acetic acid, and acetaminophen combination before reaction		
Operation:	Batch, 90 minutes/batch		
Streams:		103	104
Inlet/Outlet:		Inlet	Outlet
Temperature (°C)		19.7	46
Mass Flow (kg)		19709	19709
	Acetaminophen	538	538
	Acetic Acid	10010	10010
	Water	9160	9160
Molar Flow (kmol)		679	679
Time (min)		90	90
Volumetric Flow (m^3/min)		0.210	0.210
Design Data:			
Net Work (kW)			0
Net Heat Duty, from steam (GJ/batch)			1.57
Double-pipe heat exchanger, stainless steel interior, carbon steel exterior			
Utilities:	5 atm steam (152 °C)		
Comments:	5 atm steam turns from vapor to liquid state		
	Costs included in Appendix 7		

Reaction Preheater 2			
	Item		Heat Exchanger
	Item No.		HX-102
	No. Required		1
Function:	Heats acetic anhydride before reaction		
Operation:	Batch, 90 minutes/batch		
Streams:		108	109
Inlet/Outlet:		Inlet	Outlet
Temperature (^oC)		25	46
Mass Flow (kg)		18753	18753
	Acetic Anhydride	18753	18753
Molar Flow (kmol)		184	184
Time (min)		90	90
Volumetric Flow (m^3/min)		0.193	0.193
Design Data:			
Net Work (kW)			0
Net Heat Duty, from steam (GJ/batch)			0.65
Double-pipe heat exchanger, stainless steel interior, carbon steel exterior			
Utilities:	5 atm steam (152 ^oC)		
Comments:	5 atm steam turns from vapor to liquid state		
	Costs included in Appendix 7		

Reactor						
	Item					Reaction Vessel
	Item No.					R-101
	No. Required					4+1 spare
Function:	Contains reaction that produces acetaminophen, cools and crystallizes acetaminophen					
Operation:	Batch, 431 minutes/batch					
Streams:		106	111	113	143	114
Inlet/Outlet:		Inlet	Inlet	Inlet	Inlet	Outlet
Temperature (^oC)		46	46	25	25	15
Mass Flow (kg)		19709	18753	7159	476	46096
	Acetaminophen	538			476	10931
	Acetic Acid	10010				28132
	Water	9160				7033
	P-aminophenol			7159		
	Acetic Anhydride		18753			
Molar Flow (kmol)		678.7	183.7	65.6	3.1	931.2
Time (min)		10	10	20	5	15
Volumetric Flow (m^3/min)		0.128	1.736	0.317	0.075	2.290
Design Data:						
Net Work (kW)						12.6
Net Heat Duty, from $CaCl_2$ brine (GJ/batch)						-9.22
Vertical pressure vessel, Hastelloy						
$CaCl_2$ brine in jacket						
Agitator, Hastelloy						
Utilities:	$CaCl_2$ Brine (-30 ^oC)					
Comments:	Reactor heats to 80 ^oC then cools to 15 ^oC					
	$CaCl_2$ brine heats from -30 ^oC to -20 ^oC					
	Costs included in Appendix 7					

Nutsche Filter 1						
	Item					Filtration
	Item No.					NFD-101
	No. Required					2
Function:	Separates crystallized acetaminophen from slurry					
Operation:	Batch, 240 minutes/batch					
Streams:		117	x	x	120	126
Inlet/Outlet:		Inlet	Inlet	Inlet	Outlet	Outlet
Temperature (^oC)		15	15	15	15	15
Mass Flow (kg)		46096	4710	4710	46096	9419
	Acetaminophen	10931			1511	9419
	Acetic Acid	28132		3768	31900	
	Water	7033	4710	942	12685	
Molar Flow (kmol)		931	261	115	1245	62
Time (min)		120	30	30	180	30
Volumetric Flow (m^3/min)		0.286	0.157	0.153	0.243	0.249
Design Data:						
Net Work (kW)						0
Net Heat Duty (GJ/batch)						0
Agitated nutsche filter, Hastelloy						
Utilities:	None					
Comments:	Crystals are washed twice					
	Costs included in Appendix 7					

Solvent Preheater			
	Item		Heat Exchanger
	Item No.		HX-103
	No. Required		1
Function:	Heats solvent for recrystallization		
Operation:	Batch, 90 minutes/batch		
Streams:		152	153
Inlet/Outlet:		Inlet	Outlet
Temperature (^oC)		30.0	80
Mass Flow (kg)		36680	36680
	Acetaminophen	1145	1145
	Acetic Acid	28427	28427
	Water	7107	7107
Molar Flow (kmol)		875	875
Time (min)		90	90
Volumetric Flow (m^3/min)		0.386	0.386
Design Data:			
Net Work (kW)			0
Net Heat Duty, from steam (GJ/batch)			4.39
Double-pipe heat exchanger, stainless steel interior, carbon steel exterior			
Utilities:	5 atm steam (152 ^oC)		
Comments:	5 atm steam turns from vapor to liquid state		
	Costs included in Appendix 7		

Dissolver				
	Item			Vessel
	Item No.			V-110
	No. Required			1
Function:	Contains the dissolution of acetaminophen for recrystallization			
Operation:	Batch, 120 minutes/batch			
Streams:		127	129	130
Inlet/Outlet:		Inlet	Inlet	Outlet
Temperature (^oC)		15	80	80
Mass Flow (kg)		9419	36680	46099
	Acetaminophen	9419	1145	10565
	Acetic Acid		28427	28427
	Water		7107	7107
Molar Flow (kmol)		62	875	938
Time (min)		30	15	20
Volumetric Flow (m^3/min)		0.249	2.314	1.735
Design Data:				
Net Work (kW)				12.7
Net Heat Duty (GJ/batch)				0
Vertical pressure vessel, Hastelloy				
Agitator, Hastelloy				
Utilities:	None			
Comments:	Costs included in Appendix 7			

Granular Activated Carbon			
	Item		Adsorption
	Item No.		GAC-101
	No. Required		2
Function:	Removes impuriies from stream		
Operation:	Batch, 20 minutes/batch		
Streams:		131	132
Inlet/Outlet:		Inlet	Outlet
Temperature (°C)		80	80
Mass Flow (kg)		46099	46099
	Acetaminophen	10565	10565
	Acetic Acid	28427	28427
	Water	7107	7107
Molar Flow (kmol)		938	938
Time (min)		20	20
Volumetric Flow (m^3/min)		1.735	1.735
Design Data:			
Net Work (kW)			0
Net Heat Duty (GJ/batch)			0
Vertical pressure vessel, Hastelloy			
Utilities:	None		
Comments:	Column is switched and granular activated carbon is replaced every 8.25 day		
	Costs included in Appendix 7		

Recrystallizer				
	Item			Vessel
	Item No.			V-112
	No. Required			4+1 spare
Function:	Contains the recrystallization of acetaminophen			
Operation:	Batch, 390 minutes/batch			
Streams:		133	145	134
Inlet/Outlet:		Inlet	Inlet	Outlet
Temperature (^oC)		80	25	15
Mass Flow (kg)		46099	476	46575
	Acetaminophen	10565	476	11040
	Acetic Acid	28427		28427
	Water	7107		7107
Molar Flow (kmol)		938	3	941
Time (min)		20	5	15
Volumetric Flow (m^3/min)		1.735	0.075	2.314
Design Data:				
Net Work (kW)				0
Net Heat Duty, from $CaCl_2$ brine (GJ/batch)				-8.30
Autoclave, Hastelloy				
$CaCl_2$ brine in jacket				
Utilities:	$CaCl_2$ Brine (-30 ^oC)			
Comments:	Vessel cools from 80 ^oC to 15 ^oC			
	$CaCl_2$ Brine heats from -30 ^oC to -20 ^oC			
	Costs included in Appendix 7			

Nutsche Filter 2						
	Item					Filtration
	Item No.					NFD-102
	No. Required					6+1 spare
Function:	Separates crystallized acetaminiphen from slurry					
Operation:	Batch, 660 minutes/batch					
Streams:		137	x	x	146	140
Inlet/Outlet:		Inlet	Inlet	Inlet	Outlet	Outlet
Temperature (^oC)		15	15	15	15	15
Mass Flow (kg)		46575	4756	4756	46575	9513
	Acetaminophen	11040			1527	9513
	Acetic Acid	28427		3805	32233	
	Water	7107	4756	951	12815	
Molar Flow (kmol)		941	264	116	1258	63
Time (min)		120	30	30	180	30
Volumetric Flow (m^3/min)		0.289	0.159	0.155	0.245	0.252
Design Data:						
Net Work (kW)						0
Net Heat Duty (GJ/batch)						0
Agitated nutsche filter, Hastelloy						
Utilities:	None					
Comments:	Crystals are washed twice					
	Costs included in Appendix 7					

Distillation						
	Item					Distillation
	Item No.					V-116
	No. Required					1+1 spare
Function:	Separates the material into two streams					
Operation:	Batch, 120 minutes/batch					
Streams:		156	158	160	161	163
Inlet/Outlet:		Inlet	Inlet	Inlet	Outlet	Outlet
Temperature (^oC)		15	15	15	107	107
Mass Flow (kg)		18932	23626	9265	8133	43691
	Acetaminophen		974	382	1355	
	Acetic Acid	7573	18122	7107	5164	27637
	Water	11359	4530	1777	1613	16054
Molar Flow (kmol)		757	560	219	184	1351
Time (min)		10	10	10	20	20
Volumetric Flow (m^3/min)		1.871	2.212	0.868	0.331	2.144
Design Data:						
Net Work (kW)						0
Net Heat Duty, from steam (kW)						73.2
Net Heat Duty, from NaCl brine (GJ/batch)						-59.99
Vertical pressure vessel, Hastelloy						
Both heat exchangers are fixed head heat exchanger, stainless steel interior, carbon steel exterior						
Utilities:	NaCl Brine (-10 ^oC), 5 atm steam (152 ^oC)					
Comments:	Material gets heated to 107 ^oC to separate. Vapor material is condensed before transferring out					
	NaCl Brine heats from -10 ^oC to 0 ^oC					
	5 atm steam turns from vapor to liquid state					
	Costs included in Appendix 7					

14.2: Continuous Process

Reaction Preheater 1			
	Item		Heat Exchanger
	Item No.		HX-101
	No. Required		1
Function:	Heats water, acetic acid, and acetaminophen combination before reaction		
Operation:	Continuous		
Streams:		103	104
Inlet/Outlet:		Inlet	Outlet
Temperature (^oC)		19.7	53.7
Mass Flow (kg/min)		145.6	145.6
	Acetaminophen	4.0	4.0
	Acetic Acid	73.9	73.9
	Water	67.7	67.7
Molar Flow (kmol/min)		5.02	5.02
Volumetric Flow (m^3/min)		0.139	0.139
Design Data:			
Net Work (kW)			0
Net Heat Duty, from steam (kW)			250.085
Double-pipe heat exchanger, stainless steel interior, carbon steel exterior			
Utilities:	5 atm steam (152 ^oC)		
Comments:	5 atm steam turns from vapor to liquid state		
	Costs included in Appendix 7		

Reaction Preheater 2			
	Item		Heat Exchanger
	Item No.		HX-102
	No. Required		1
Function:	Heats acetic anhydride before reaction		
Operation:	Continuous		
Streams:		106	107
Inlet/Outlet:		Inlet	Outlet
Temperature (^oC)		25	53.7
Mass Flow (kg/min)		138.7	138.7
	Acetic Anhydride	138.7	138.7
Molar Flow (kmol/min)		1.36	1.36
Volumetric Flow (m^3/min)		0.128	0.128
Design Data:			
Net Work (kW)			0
Net Heat Duty, from steam (kW)			109.155
Double-pipe heat exchanger, stainless steel interior, carbon steel exterior			
Utilities:	5 atm steam (152 ^oC)		
Comments:	5 atm steam turns from vapor to liquid state		
	Costs included in Appendix 7		

CSTR 1					
	Item				Reaction Vessel
	Item No.				R-101
	No. Required				1+1 spare
Function:	First for the reactions to occur in				
Operation:	Continuous				
Streams:		104	107	109	110
Inlet/Outlet:		Inlet	Inlet	Inlet	Outlet
Temperature (^{o}C)		53.7	53.7	25	80
Mass Flow (kg/min)		145.6	138.7	52.9	337.2
	Acetaminophen	4.0			75.8
	Acetic Acid	73.9			189.4
	Water	67.7			54.7
	P-aminophenol			53.0	1.1
	Acetic Anhydride		138.7		16.3
Molar Flow (kmol/min)		5.02	1.36	0.49	6.86
Volumetric Flow (m^3/min)		0.139	0.128	0.047	0.254
Design Data:					
Net Work (kW)					2.8
Net Heat Duty (kW)					0
Vertical pressure vessel, Hastelloy					
Agitator, Hastelloy					
Utilities:	None				
Comments:	Reaction heats inlets to 80 ^{o}C				
	Costs included in Appendix 7				

CSTR 2			
	Item		Reaction Vessel
	Item No.		R-102
	No. Required		1
Function:	Second for the reactions to occur in		
Operation:	Continuous		
Streams:		111	112
Inlet/Outlet:		Inlet	Outlet
Temperature (°C)		80	80
Mass Flow (kg/min)		337.2	337.2
	Acetaminophen	75.8	77.3
	Acetic Acid	189.4	207.9
	Water	54.7	52.0
	P-aminophenol	1.1	
	Acetic Anhydride	16.3	
Molar Flow (kmol/min)		6.86	6.86
Volumetric Flow (m^3/min)		0.254	0.254
Design Data:			
Net Work (kW)			3.3
Net Heat Duty, from NaCl brine (kW)			-326
Vertical pressure vessel, Hastelloy			
NaCl brine in jacket			
Agitator, Hastelloy			
Utilities:	NaCl Brine (-10 °C)		
Comments:	NaCl brine removes energy released from reaction to maintain 80 °C		
	NaCl brine heats from -10 °C to 0 °C		
	Costs included in Appendix 7		

Crystallizer 1			
	Item		Vessel
	Item No.		V-105
	No. Required		1+1 spare
Function:	Contains the recrystallization of acetaminophen		
Operation:	Continuous		
Streams:		113	114
Inlet/Outlet:		Inlet	Outlet
Temperature (^oC)		80	42
Mass Flow (kg/min)		337.2	337.2
	Acetaminophen	77.3	77.3
	Acetic Acid	207.9	207.9
	Water	52.0	52.0
Molar Flow (kmol/min)		6.86	6.86
Volumetric Flow (m^3/min)		0.254	0.254
Design Data:			
Net Work (kW)			29.5
Net Heat Duty, from $CaCl_2$ brine (kW)			-629
Vertical pressure vessel, Hastelloy			
$CaCl_2$ brine in jacket			
Agitator, Hastelloy			
Utilities:	$CaCl_2$ Brine (-30 ^oC)		
Comments:	Vessel cools from 80 ^oC to 42 ^oC		
	$CaCl_2$ Brine heats from -30 ^oC to -20 ^oC		
	Costs included in Appendix 7		

Crystallizer 2			
	Item		Vessel
	Item No.		V-106
	No. Required		1
Function:	Contains the recrystallization of acetaminophen		
Operation:	Continuous		
Streams:		115	116
Inlet/Outlet:		Inlet	Outlet
Temperature (^oC)		42	15
Mass Flow (kg)		337.2	337.2
	Acetaminophen	77.3	77.3
	Acetic Acid	207.9	207.9
	Water	52.0	52.0
Molar Flow (kmol)		6.86	6.86
Volumetric Flow (m^3/min)		0.254	0.254
Design Data:			
Net Work (kW)			29.7
Net Heat Duty, from $CaCl_2$ brine (kW)			-376
Vertical pressure vessel, Hastelloy			
$CaCl_2$ brine in jacket			
Agitator, Hastelloy			
Utilities:	$CaCl_2$ Brine (-30 ^oC)		
Comments:	Vessel cools from 42 ^oC to 15 ^oC		
	$CaCl_2$ Brine heats from -30 ^oC to -20 ^oC		
	Costs included in Appendix 7		

Screw Press Filter 1							
	Item						Filtration
	Item No.						SP-101
	No. Required						1+1 spare
Function:	Separates crystallized acetaminophen from slurry						
Operation:	Continuous						
Streams:		117	x	x	120	151	124
Inlet/Outlet:		Inlet	Inlet	Inlet	Outlet	Outlet	Outlet
Temperature (°C)		15	15	15	15	15	15
Mass Flow (kg/min)		337.2	33.0	33.0	271.1	66.1	66.1
	Acetaminophen	77.3			11.2		66.1
	Acetic Acid	207.9		26.4	207.9	26.4	
	Water	52.0	33.0	6.6	52.0	39.7	
Molar Flow (kmol/min)		6.86	1.83	0.81	6.42	2.64	0.44
Volumetric Flow (m^3/min)		0.254	0.033	0.032	0.254	0.065	0.052
Design Data:							
Net Work (kW)							0
Net Heat Duty (kW)							0
Screw press filter, Hastelloy							
Utilities:	None						
Comments:	Crystals are washed twice						
	Costs included in Appendix 7						

Solvent Preheater			
	Item		Heat Exchanger
	Item No.		HX-103
	No. Required		1
Function:	Heats solvent for recrystallization		
Operation:	Continuous		
Streams:		147	148
Inlet/Outlet:		Inlet	Outlet
Temperature (°C)		30.2	80
Mass Flow (kg/min)		257.4	257.4
	Acetaminophen	8.0	8.0
	Acetic Acid	199.5	199.5
	Water	49.9	49.9
Molar Flow (kmol/min)		6.14	6.14
Volumetric Flow (m^3/min)		0.244	0.244
Design Data:			
Net Work (kW)			0
Net Heat Duty, from steam (kW)			522.208
Double-pipe heat exchanger, stainless steel interior, carbon steel exterior			
Utilities:	5 atm steam (152 °C)		
Comments:	5 atm steam turns from vapor to liquid state		
	Costs included in Appendix 7		

Dissolver				
	Item			Vessel
	Item No.			V-107
	No. Required			1
Function:	Contains the dissolution of acetaminophen for recrystallization			
Operation:	Continuous			
Streams:		125	148	126
Inlet/Outlet:		Inlet	Inlet	Outlet
Temperature (^oC)		15	80	80
Mass Flow (kg/min)		66.1	257.4	323.5
	Acetaminophen	66.1	8.0	74.1
	Acetic Acid		199.5	199.5
	Water		49.9	49.9
Molar Flow (kmol/min)		0.44	6.14	6.58
Volumetric Flow (m^3/min)		0.052	0.244	0.244
Design Data:				
Net Work (kW)				0
Net Heat Duty (kW)				0
Vertical pressure vessel, Hastelloy				
Agitator, Hastelloy				
Utilities:	None			
Comments:	Costs included in Appendix 7			

Granular Activated Carbon			
	Item		Adsorption
	Item No.		GAC-101
	No. Required		2
Function:	Removes impurities from stream		
Operation:	Continuous		
Streams:		127	128
Inlet/Outlet:		Inlet	Outlet
Temperature (°C)		80	80
Mass Flow (kg/min)		323.5	323.5
	Acetaminophen	74.1	74.1
	Acetic Acid	199.5	199.5
	Water	49.9	49.9
Molar Flow (kmol/min)		6.58	6.58
Volumetric Flow (m^3/min)		0.244	0.244
Design Data:			
Net Work (kW)			0
Net Heat Duty (kW)			0
Vertical pressure vessel, Hastelloy			
Utilities:	None		
Comments:	Column is switched and granular activated carbon is replaced every 2.9 day		
	Costs included in Appendix 7		

Recrystallizer 1			
	Item		Vessel
	Item No.		V-108
	No. Required		1+1 spare
Function:	Contains the recrystallization of acetaminophen		
Operation:	Continuous		
Streams:		129	130
Inlet/Outlet:		Inlet	Outlet
Temperature (°C)		80	42
Mass Flow (kg)		323.5	323.5
	Acetaminophen	74.1	74.1
	Acetic Acid	199.5	199.5
	Water	49.9	49.9
Molar Flow (kmol)		6.58	6.58
Volumetric Flow (m^3/min)		0.244	0.244
Design Data:			
Net Work (kW)			27.7
Net Heat Duty, from $CaCl_2$ brine (kW)			-604
Vertical pressure vessel, Hastelloy			
$CaCl_2$ brine in jacket			
Agitator, Hastelloy			
Utilities:	$CaCl_2$ Brine (-30 C°)		
Comments:	Vessel cools from 80 °C to 42 °C		
	$CaCl_2$ Brine heats from -30 °C to -20 °C		
	Costs included in Appendix 7		

Recrystallizer 2			
	Item		Vessel
	Item No.		V-109
	No. Required		1
Function:	Contains the recrystallization of acetaminophen		
Operation:	Continuous		
Streams:		131	132
Inlet/Outlet:		Inlet	Outlet
Temperature (^oC)		42	15
Mass Flow (kg)		323.5	323.5
	Acetaminophen	74.1	74.1
	Acetic Acid	199.5	199.5
	Water	49.9	49.9
Molar Flow (kmol)		6.58	6.58
Volumetric Flow (m^3/min)		0.244	0.244
Design Data:			
Net Work (kW)			27.9
Net Heat Duty, from $CaCl_2$ brine (kW)			-361
Vertical pressure vessel, Hastelloy			
$CaCl_2$ brine in jacket			
Agitator, Hastelloy			
Utilities:	$CaCl_2$ Brine (-30 ^oC)		
Comments:	Vessel cools from 42 ^oC to 15 ^oC		
	$CaCl_2$ Brine heats from -30 ^oC to -20 ^oC		
	Costs included in Appendix 7		

Screw Press Filter 2							
	Item						Filtration
	Item No.						SP-102
	No. Required						1+1 spare
Function:	Separates crystallized acetaminophen from slurry						
Operation:	Continuous						
Streams:		133	x	x	142	155	136
Inlet/Outlet:		Inlet	Inlet	Inlet	Outlet	Outlet	Outlet
Temperature (°C)		15	15	15	15	15	15
Mass Flow (kg/min)		323.5	31.7	31.7	260.1	63.4	63.4
	Acetaminophen	74.1			10.7		63.4
	Acetic Acid	199.5		25.4	199.5	25.4	
	Water	49.9	31.7	6.3	49.9	38.1	
Molar Flow (kmol/min)		6.58	1.76	0.77	6.16	2.53	0.42
Volumetric Flow (m^3/min)		0.244	0.032	0.031	0.244	0.063	0.050
Design Data:							
Net Work (kW)							0
Net Heat Duty (kW)							0
Screw press filter, Hastelloy							
Utilities:	None						
Comments:	Crystals are washed twice						
	Costs included in Appendix 7						

Fluid Bed Dryer			
	Item		Fluid Bed Dryer
	Item No.		FBDR-101
	No. Required		1+1 spare
Function:	Dries material going through it		
Operation:	Continuous		
Streams:		137	140
Inlet/Outlet:		Inlet	Outlet
Temperature (^oC)		15	
Mass Flow (kg/min)		63.4	63.4
	Acetaminophen	63.4	63.4
	Acetic Acid		
	Water		
Molar Flow (kmol/min)		0.42	0.42
Volumetric Flow (m^3/min)		0.050	0.050
Design Data:			
Net Work (kW)			0
Net Heat Duty (kW)			0
Utilities:	None		
Comments:	Costs included in Appendix 7		

Distillation				
	Item			Distillation
	Item No.			C-101
	No. Required			1+1 spare
Function:	Separates the material into two streams			
Operation:	Continuous			
Streams:		158	159	161
Inlet/Outlet:		Inlet	Outlet	Outlet
Temperature (^oC)		15	107	107
Mass Flow (kg/min)		369.3	59.3	310.0
	Acetaminophen	9.9	9.9	
	Acetic Acid	235.7	37.6	198.1
	Water	123.7	11.8	111.9
Molar Flow (kmol/min)		10.86	1.34	9.51
Volumetric Flow (m^3/min)		0.353	0.048	0.304
Design Data:				
Net Work (kW)				0
Net Heat Duty, from steam (kW)				8,607
Net Heat Duty, from NaCl brine (kW)				-7,048
Vertical pressure vessel, Hastelloy				
Both heat exchangers are fixed head heat exchanger, stainless steel interior, carbon steel exterior				
Utilities:	NaCl Brine (-10 ^oC), 5 atm steam (152 ^oC)			
Comments:	Material gets heated to 107 ^oC to separate. Vapor material is condensed before transfer.			
	NaCl Brine heats from -10 ^oC to 0 ^oC			
	5 atm steam turns from vapor to liquid state			
	Costs included in Appendix 7			

Section 15: Equipment Cost Summary

15.1: Batch Equipment Costs

The purchase cost of the major process equipment in the batch process is shown in Table 17.1. The complete costing process that includes the detailed use of Seider et. Al Chapter 16 and 17 is presented in A.7.

Table 15.1 Batch Equipment Cost

Equipment Description	Process Type	Bare-Module Cost
Water Storage	Fab Eq	1,000,439.57
P-A storage	Fab Eq	862,530.86
AA storage	Fab Eq	1,772,265.11
Heated Storage H2O	Fab Eq	1,936,814.48
Heated Storage AA	Fab Eq	1,930,695.55
Reactor 1 (4)	Fab Eq	14,526,714.16
Storage	Fab Eq	3,800,644.96
Agitated Nutsche Filter	Fab Eq	3,298,423.97
P4 heating dissolving	Fab Eq	3,763,146.97
Storage	Fab Eq	1,898,654.74
Fluid Bed Carbon	Fab Eq	2,104,677.69
Crystallizer	Fab Eq	4,305,712.76
Storage	Fab Eq	2,039,735.72
ANF2	Fab Eq	9,376,757.26
Storage	Fab Eq	1,560,985.65
Storage	Fab Eq	1,133,817.84
Batch Distillation	Fab Eq	2,981,902.47
Storage	Fab Eq	1,016,119.71
Storage	Fab Eq	2,318,274.94
Storage	Fab Eq	1,228,696.26
Pumps	Proc Mach	4,541,177.09
Total		**67,398,187.75**

15.2: Continuous Equipment Costs

Table 15.2 Continuous Equipment Cost

Equipment Description	Process Type	Bare-Module Cost	
Water Storage	Fab Eq	215,234.44	
P-A storage	Fab Eq	186,598.03	
AA storage	Fab Eq	594,673.52	
Heat exchanger PA	Fab Eq	9,659.50	
Heat exchanger AA	Fab Eq	8,488.57	
Reactor 1 (CSTR)	Fab Eq	2,054,183.19	
Reactor 2 (CSTR)	Fab Eq	2,188,344.40	
Reactor 3 (MSMPR)	Fab Eq	5,421,251.09	
Reactor 4 (MSMPR)	Fab Eq	5,435,583.15	
Screw Press	Fab Eq	2,246,361.18	
CSTR dissolving	Fab Eq	561,796.27	
Carbon Treatment	Fab Eq	85,581.33	
Reactor 6 (MSMPR)	Fab Eq	5,274,546.87	
Reactor 7 (MSMPR)	Fab Eq	5,288,375.86	
Screw Press	Fab Eq	1,356,952.49	
Fluid Bed Drying	Fab Eq	1,831,634.65	
Distillation	Fab Eq	1,068,967.26	
Bottoms Storage	Fab Eq	948,668.71	
Tops Storage	Fab Eq	2,136,547.64	
Pumps	Proc Mach	3108722	
Total			**40,022,169.94**

Section 16: Economic Assumptions

16.1: Total Capital Investment Assumptions

From the total equipment cost outlined in Section 17, several assumptions were made to reach the total capital investment. As the plant will operate in India, a site factor of 0.85 was applied.

Table 16.1: Assumptions and totals to reach Batch Total Permanent Investment

Assumptions	Abbv.	Title	Cost
A7	Cfe	TBM fabricated eq	40,357,335.28
A7	Cpm	TBM process machinery	4,541,177.09
A7	Cspare	TBM spares	10,639,563.31
A7	Cstorage	TBM storage and surge	20,601,020.64
None	Ccatalyst	Cost Catalyst	0.00
None	Ccomp	TBM computers, software etc.	0.00
	CTBM	Total Bare Module Investment	**76,139,096.32**
5% CTBM	Csite	Cost site prep	3,806,954.82
5% CTBM	Cserv	cost service fac	3,806,954.82
None	Calloc	Allocated cost	0.00
	CDPI	Total direct permanent invest	**83,753,005.95**

Table 16.2: Assumptions and totals to reach Continuous Total Permanent Investment

Assumptions	Abbv.	Title	Cost
A7	Cfe	TBM fabricated eq	32,842,927.32
A7	Cpm	TBM process machinery	3,372,476.43
A7	Cspare	TBM spares	25,774,925.50
A7	Cstorage	TBM storage and surge	4,081,722.34
None	Ccatalyst	Cost Catalyst	0.00
None	Ccomp	TBM computers, software etc.	0.00
	CTBM	Total Bare Module Investment	66,072,051.59
5% CTBM	Csite	Cost site prep	3,303,602.58
5% CTBM	Cserv	cost service fac	3,303,602.58
None	Calloc	Allocated cost	0.00
	CDPI	Total direct permanent invest	72,679,256.75

The quantity of spares for each process unit was determined with consultants to ensure conservative securities were in place for any malfunctions or damages. A description on decision making is outlined in A7. To reach total capital investment, Tables 18.3 and 18.4 outline the assumptions made.

Table 16.3: Assumptions and totals to reach Batch Total Capital Investment

Assumptions	Abbv.	Title	Cost
18% CDPI	C cont	Const of contingencies	15,075,541.07
	CTDC	Total depreciable capital	98,828,547.02
2% TDC	Cland	cost of land	1,976,570.94
None	Croyal	cost of royalties	0.00
10% TDC	Cstartup	cost plant startup	9,882,854.70
	CTPI	total permanent investment	110,687,972.67
15% TPI	Cwc	working capital	16,603,195.90
	Ctci	total capital investment	127,291,168.57

Table 16.3: Assumptions and totals to reach Continuous Total Capital Investment

Assumptions	Abbv.	Title	Cost
18% CDPI	C cont	Const of contingencies	15,075,541.07
	CTDC	Total depreciable capital	98,828,547.02
2% TDC	Cland	cost of land	1,976,570.94
None	Croyal	cost of royalties	0.00
10% TDC	Cstartup	cost plant startup	9,882,854.70
	CTPI	total permanent investment	110,687,972.67
15% TPI	Cwc	working capital	16,603,195.90
	Ctci	total capital investment	127,291,168.57

16.2: Fixed Cost Assumptions

Table 16.4 Operations Batch

	Details		Cost
Operators Per Shift	12.00	(assuming 5 shifts)	
Direct Wages and Benefits (DW&B)	40.00	/operator/hour	3,363,840.00
Direct Salaries and Benefits	15%	of DW&B	504,576.00
Operating Supplies and Services	6%	of DW&B	201,830.40
Technical Assistance to Manufacturing	60,000.00	/yr/operator/shift	720,000.00
Control Laboratory	65,000.00	/yr/operator/shift	780,000.00
SUM			5,570,246.40

Table 16.5 Maintenance Batch

	Details		Cost
Wages and Benefits (MW&B)	4.50%	of TDC	4,447,284.62
Salaries and Benefits	25%	of MW&B	1,111,821.15
Materials and Services	100%	of MW&B	4,447,284.62
Maintenance Overhead	5%	of MW&B	222,364.23
Solids-Fluid Handling Process	4.50%	of C(TDC)	4,447,284.62
SUM			14,676,039.23

Table 16.6 Overhead Batch

	Details		Cost
General Plant Overhead	7.10%	of M&O	554,589.85
Mechanical Department Services	2.40%	of M&O	187,466.99
Employee Relations Department	5.90%	of M&O	460,856.35
Business Services	7.40%	of M&O	578,023.22
SUM			1,780,936.41

Table 16.7 Depreciation Batch

	Details		**Cost**
Direct Plant	8 %	of (CTDC – 1.18 Calloc)	7,906,283.76
Allocated Plant	6 %	of 1.18Calloc	0.00
Rental Fees			0.00
Licensing Fees			0.00
SUM			7,906,283.76

Table 16.8 Operations Continuous

	Details		Cost
Operators Per Shift	9.00	(assuming 5 shifts)	0.00
Direct Wages and Benefits (DW&B)	40.00	/operator/hour	2,522,880.00
Direct Salaries and Benefits	15%	of DW&B	378,432.00
Operating Supplies and Services	6%	of DW&B	151,372.80
Technical Assistance to Manufacturing	60,000.00	/yr/operator/shift	540,000.00
Control Laboratory	65,000.00	/yr/operator/shift	585,000.00
SUM			4,177,684.80

Table 16.9 Maintenance Continuous

	Details		Cost
Wages and Benefits (MW&B)	4.50%	of TDC	3,859,268.53
Salaries and Benefits	25%	of MW&B	964,817.13
Materials and Services	100%	of MW&B	3,859,268.53
Maintenance Overhead	5%	of MW&B	192,963.43
Solids-Fluid Handling Process	4.50%	of C(TDC)	3,859,268.53
SUM			12,735,586.16

Table 16.10 Overhead Continuous

	Details		Cost
General Plant Overhead	7.10%	of M&O	453,132.55
Mechanical Department Services	2.40%	of M&O	153,171.56
Employee Relations Department	5.90%	of M&O	376,546.76
Business Services	7.40%	of M&O	472,278.99
SUM			1,455,129.87

Table 16.11 Depreciation Continuous

	Details		Cost
Direct Plant	8 %	of (CTDC – 1.18 Calloc)	6,860,921.84
Allocated Plant	6 %	of 1.18Calloc	0.00
Rental Fees			0.00
Licensing Fees			0.00
SUM			6,860,921.84

When comparing batch to continuous, one of the major expense differences lies with the operators. Continuous demands fewer operators on the order of $1 Million per year. As the following assumptions for fixed costs followed as percentages on total capital investment, continuous was uniformly less expensive.

16.3: Working Capital Assumptions

Table 16.12 Working Capital Batch

Account Receivable	**30**	**Days**	**12328767.12**
Cash Reserves	0	Days	0
Accounts Payable	0	Days	0
Acetaminophen Inventory	4	Days	1,643,835.616
Raw Materials	2	Days	1,082,019.571
Sum			15,054,622.31

Table 16.13 Working Capital Continuous

Account Receivable	**30**	**Days**	**12,328,767.12**
Cash Reserves	0	Days	0.00
Accounts Payable	0	Days	0.00
Acetaminophen Inventory	4	Days	1,643,835.62
Raw Materials	2	Days	945,447.85
Total			14,918,050.59

Tables 16.12 and 16.13 demonstrate working capital needs 100% capacity. This is modified in the input summary in Section 17 to reflect the business cycle. It is important to note that limiting cash reserves to none is a conservative approach held for both processes. This could improve profitability if included.

Section 17: Batch Profitability Analysis

17.1: Input Summary

General Information

Process Title:	**Batch Process**
Product:	**Acetaminophen Powder**
Plant Site Location:	**India**
Site Factor:	**0.8**
Operating Hours per Year:	**7008**
Operating Days per Year:	**292**
Operating Factor:	**0.9041**

Process Information

This Process will Yield

4.28	Metric Tons of Acetaminophen per hour
102.74	Metric Tons of Acetaminophen per day
30,000	Metric Tons of Acetaminophen per year

Price	$4.00	**/kg**

Chronology

Year	**Action**	**Distribution of Permanent Investment**	**Production Capacity**	**Depreciation**	**Product Price**
2022	Design		0%		
2023	Construction	100%	0%	20.00%	$4.00
2024	Production		45.0%	32.00%	$4.00
2025	Production		67.5%	19.20%	$4.00
2026	Production		90.0%	11.52%	$4.00
2027	Production		90.0%	11.52%	$4.00
2028	Production		90.0%	05.76%	$4.00
2029	Production		90.0%		$4.00
2030	Production		90.0%		$4.00
2031	Production		90.0%		$4.00
2032	Production		90.0%		$4.00
2033	Production		90.0%		$4.00
2034	Production		90.0%		$4.00
2035	Production		90.0%		$4.00
2036	Production		90.0%		$4.00
2037	Production		90.0%		$4.00

Equipment Costs

Equipment Description		Bare-Module Costs
Reactor Vessels	Fabricated Equipment	$14,500,000
Crystallizers	Fabricated Equipment	$4,300,000
Filters and Adsorbers	Fabricated Equipment	$14,800,000
Distillation Column	Fabricated Equipment	$3,000,000
Storage Tanks	Fabricated Equipment	$26,300,000
Pumps	Process Machinery	$4,500,000
Total		**$67,400,000**

Raw Materials

Raw Materials:	Unit:	Required Ratio:	Cost of Raw Material:
p-Aminophenol	kg	0.85 kg per kg of Acetaminophen	$1.2 per kg
Acetic Anhydride	kg	2.19 kg per kg of Acetaminophen	$1.5 per kg
Water	kg	0.78 kg per kg of Acetaminophen	$0.000211 per kg
Total weighted Average:			**$4.31 per kg of Acetaminophen**

Byproduct

Byproduct:	Unit:	Ratio to Product:	Byproduct Selling Price:
Acetic Acid	kg	3.23 kg per kg of Acetaminophen	$1 per kg
Total weighted Average:			**$3.23 per kg of Acetaminophen**

Utilities

Total weighted Average: **$0.33 per kg of Acetaminophen**

17.2: Investment Summary

Investment Summary		
Bare Module Costs		
Fabricated Equipment	$40,400,000	
Process Machinery	$4,500,000	
Spares	$10,600,000	
Storage	$20,600,000	
Other Equipment	$0	
Catalysts	$0	
Computers, Software, Etc.	$0	
Total Bare Module Costs:		**$76,100,000**
Direct Permanent Investment		
Cost of Site Preparations	$3,800,000	
Cost of Service Facilities	$3,800,000	
Allocated Costs for Utility Plants and Related Facilities	$0	
Direct Permanent Investment:		**$83,700,000**
Total Depreciable Capital		
Cost of Contingencies & Contractor Fees	$15,100,000	
Total Depreciable Capital:		**$98,800,000**
Total Permanent Investment		
Cost of Land	$2,000,000	
Cost of Royalties	$0	
Cost of Plant Start-Up	$9,900,000	
Total Permanent Investment:		**$110,700,000**
Total Capital Investment		
Working Capital		$16,600,000
Total Capital Investment		**$127,300,000**

17.3: Variable Cost Summary

Variable Cost Summary

Variable Costs at 100% Capacity:

General Expenses

Selling / Transfer Expenses:		$6,690,000
Direct Research:		$10,700,000
Allocated Research:		$1,100,000
Administrative Expense:		$4,500,000
Management Incentive Compensation:		$2,800,000
		$25,800,000
Total General Expenses		
Raw Materials	$5.3 per kg of Acetaminophen	$158,000,000
Byproducts	$3.9 per kg of Acetaminophen	-$118,000,000
Utilities	$0.33 per kg of Acetaminophen	$9,900,000
Total Variable Costs		**$75,500,000**

17.4: Fixed Cost Summary

Fixed Cost Summary	
<u>Operations</u>	
Direct Wages and Benefits	$3,930,000
Direct Salaries and Benefits	$590,000
Operating Supplies and Services	$240,000
Technical Assistance to Manufacturing	$840,000
Control Laboratory	$910,000
Total Operations:	**$6,500,000**
<u>Maintenance</u>	
Wages and Benefits	$4,450,000
Salaries and Benefits	$1,100,000
Materials and Services	$4,450,000
Maintenance Overhead	$220,000
Solids-Fluid Handling Process	$4,450,000
Total Maintenance:	**$14,700,000**
<u>Operating Overhead</u>	
General Plant Overhead	$550,000
Mechanical Department Services	$190,000
Employee Relations Department	$460,000
Business Services	$580,000
Total Operating Overhead:	**$1,780,000**
<u>Property Taxes and Insurances</u>	
Property Taxes and Insurance	
<u>Other Annual Expenses</u>	
Rental Fees (Office and Laboratory Space)	$0
Licensing Fees	$0
Miscellaneous	$0
Total Other Annual Expenses:	**$7,900,000**
<u>Total Fixed Costs:</u>	**$30,800,000**

17.5: Cash Flow Summary

Cash Flow Summary ('000)

Year	Prod. Capacity	Price	Sales	Capital Cost	Working Capital	Var Cost	Fixed Cost	Depreciation (5 yr MACRS)	Depletion Allowance	Taxable Income	Taxes	Net Earnings	Cash Flow	Discounted Cash Flow	Cumulative NPV 15%
2,022	0		0	(34,500)	(6,800)	0	0	0	0	0	0	0	(41,300)	(41,300)	**(41,300)**
2,023	0	4	54,000		(3,400)	(34,000)	(13,900)	(19,800)	0	(13,600)	0	(13,600)	2,800	2,400	**(38,900)**
2,024	1	4	81,000		(3,400)	(51,000)	(20,800)	(31,600)	0	(22,400)	0	(22,400)	5,800	4,400	**(34,500)**
2,025	1	4	108,000		0	(67,900)	(27,800)	(19,000)	0	(6,700)	0	(6,700)	12,300	8,100	**(26,500)**
2,026	1	4	108,000		0	(67,900)	(27,800)	(11,400)	0	900	400	500	11,900	6,800	**(19,600)**
2,027	1	4	108,000		0	(67,900)	(27,800)	(11,400)	0	900	400	500	11,900	5,900	**(13,700)**
2,028	1	4	108,000		0	(67,900)	(27,800)	(5,700)	0	6,600	2,600	4,000	9,600	4,200	**(9,500)**
2,029	1	4	108,000		0	(67,900)	(27,800)		0	12,300	4,900	7,400	7,400	2,800	**(6,800)**
2,030	1	4	108,000		0	(67,900)	(27,800)		0	12,300	4,900	7,400	7,400	2,400	**(4,400)**
2,031	1	4	108,000		0	(67,900)	(27,800)		0	12,300	4,900	7,400	7,400	2,100	**(2,300)**
2,032	1	4	108,000		0	(67,900)	(27,800)		0	12,300	4,900	7,400	7,400	1,800	**(500)**
2,033	1	4	108,000		0	(67,900)	(27,800)		0	12,300	4,900	7,400	7,400	1,600	**1,100**
2,034	1	4	108,000		0	(67,900)	(27,800)		0	12,300	4,900	7,400	7,400	1,400	**2,500**
2,035	1	4	108,000		0	(67,900)	(27,800)		0	12,300	4,900	7,400	7,400	1,200	**3,700**
2,036	1	4	108,000		0	(67,900)	(27,800)		0	12,300	4,900	7,400	7,400	1,000	**4,700**
2,037	1	4	108,000		13,500	(67,900)	(27,800)		0	12,300	4,900	7,400	20,900	2,600	**7,300**

17.6: Profitability Measures

Profitability Measures		
The Internal Rate of Return (IRR) for this project is		31.18%
The Net Present Value (NPV) of this project in 2037 is		$7,310,000
ROI Analysis (Third Production Year)		
Annual Sales	$108,000,000	
Annual Costs	$(95,700,000)	
Depreciation	$(7,050,000)	
Income Tax	$(4,900,000)	
Net Earnings	$7,400,000	
Total Capital Investment	$127,300,000	
ROI	5.7%	

17.7: Sensitivity Analysis

		Variable Costs				
		$37800000	$56700000	$75500000	$94400000	$113300000
Price	2	Negative IRR	Negative IRR	Negative IRR	Negative IRR	Negative IRR
	3	31.24%	Negative IRR	Negative IRR	Negative IRR	Negative IRR
	4	64.04%	43.16%	18.23%	Negative IRR	Negative IRR
	5	85.12%	70.15%	53.71%	31.68%	4.31%
	6	103.25%	89.66%	75.57%	60.76%	42.48%

		Fixed Costs				
		15200000	22800000	30400000	38000000	45600000
Price	2	Negative IRR	Negative IRR	Negative IRR	Negative IRR	Negative IRR
	3	Negative IRR	Negative IRR	Negative IRR	Negative IRR	Negative IRR
	4	38.94%	29.28%	18.23%	4.76%	Negative IRR
	5	67.33%	60.86%	53.71%	44.81%	35.78%
	6	87.13%	81.40%	75.57%	69.63%	63.53%

Section 18: Continuous Profitability Analysis

18.1: Input Summary

General Information

Process Title:	**Continuous Process**
Product:	**Acetaminophen Powder**
Plant Site Location:	**India**
Site Factor:	**0.85**
Operating Hours per Year:	**7008**
Operating Days per Year:	**292**
Operating Factor:	**0.9041**

Process Information

This Process will Yield

	4.28	Metric Tons of Acetaminophen per hour
	102.74	Metric Tons of Acetaminophen per day
	30,000	Metric Tons of Acetaminophen per year
Price	$4	/kg

Chronology

Year	Action	Distribution of Permanent Investment	Production Capacity	Depreciation	Product Price
2022	Design		0%		
2023	Construction	100%	0%	20.00%	$4.00
2024	Production		45.0%	32.00%	$4.00
2025	Production		67.5%	19.20%	$4.00
2026	Production		90.0%	11.52%	$4.00
2027	Production		90.0%	11.52%	$4.00
2028	Production		90.0%	05.76%	$4.00
2029	Production		90.0%		$4.00
2030	Production		90.0%		$4.00
2031	Production		90.0%		$4.00
2032	Production		90.0%		$4.00
2033	Production		90.0%		$4.00
2034	Production		90.0%		$4.00
2035	Production		90.0%		$4.00
2036	Production		90.0%		$4.00
2037	Production		90.0%		$4.00

Equipment Costs

Equipment Description		**Bare-Module Costs**
Reactor Vessels	Fabricated Equipment	$4,200,000
Crystallizers	Fabricated Equipment	$21,400,000
Filters, Adsorbers and Dryers	Fabricated Equipment	$5,500,000
Distillation Column	Fabricated Equipment	$1,100,000
Storage Tanks	Fabricated Equipment	$4,100,000
Pumps	Process Machinery	$3,100,000
Total		**$40,000,000**

Raw Materials

Raw Materials:	**Unit:**	**Required Ratio:**	**Cost of Raw Material:**
p-Aminophenol	kg	0.83 kg per kg of Acetaminophen	$1.2 per kg
Acetic Anhydride	kg	2.18 kg per kg of Acetaminophen	$1.5 per kg
Water	kg	0.78 kg per kg of Acetaminophen	$0.000211 per kg
Total weighted Average:			**$4.27 per kg of Acetaminophen**

Byproduct

Byproduct:	**Unit:**	**Ratio to Product:**	**Byproduct Selling Price:**
Acetic Acid	kg	3.18 kg per kg of Acetaminophen	$1.0 per kg
Total weighted Average:			**$3.18 per kg of Acetaminophen**

Utilities

Total weighted Average:	**$0.32 per kg of Acetaminophen**

18.2: Investment Summary

Investment Summary		
<u>Bare Module Costs</u>		
Fabricated Equipment	$32,800,000	
Process Machinery	$3,300,000	
Spares	$25,800,000	
Storage	$4,100,000	
Other Equipment	$0	
Catalysts	$0	
Computers, Software, Etc.	$0	
Total Bare Module Costs:		**$66,100,000**
<u>Direct Permanent Investment</u>		
Cost of Site Preparations	$3,300,000	
Cost of Service Facilities	$3,300,000	
Allocated Costs for Utility Plants and Related Facilities	$0	
Direct Permanent Investment:		**$72,700,000**
<u>Total Depreciable Capital</u>		
Cost of Contingencies & Contractor Fees	$13,100,000	
Total Depreciable Capital:		**$85,800,000**
<u>Total Permanent Investment</u>		
Cost of Land	$1,700,000	
Cost of Royalties	$0	
Cost of Plant Start-Up	$8,600,000	
Total Permanent Investment:		**$96,100,000**
<u>Total Capital investment</u>		
Working Capital		$14,400,000
Total Capital Investment		**$110,500,000**

18.3: Variable Cost Summary

Variable Cost Summary

Variable Costs at 100% Capacity:

General Expenses

Selling / Transfer Expenses:	$6,690,000	
Direct Research:	$10,700,000	
Allocated Research:	$1,100,000	
Administrative Expense:	$4,500,000	
Management Incentive Compensation:	$2,800,000	
		$25,800,000

Total General Expenses

Raw Materials	$4.6 per kg of Acetaminophen	$138,000,000
Byproducts	$3.4 per kg of Acetaminophen	-$101,000,000
Utilities	$0.32 per kg of Acetaminophen	$9,600,000
Total Variable Costs		**$72,600,000**

18.4: Fixed Cost Summary

Fixed Cost Summary	
<u>Operations</u>	
Direct Wages and Benefits	$2,800,000
Direct Salaries and Benefits	$420,000
Operating Supplies and Services	$170,000
Technical Assistance to Manufacturing	$600,000
Control Laboratory	$650,000
Total Operations:	**$4,600,000**
<u>Maintenance</u>	
Wages and Benefits	$3,900,000
Salaries and Benefits	$1,000,000
Materials and Services	$3,900,000
Maintenance Overhead	$190,000
Solids-Fluid Handling Process	$3,900,000
Total Maintenance:	**$12,800,000**
<u>Operating Overhead</u>	
General Plant Overhead	$450,000
Mechanical Department Services	$150,000
Employee Relations Department	$380,000
Business Services	$470,000
Total Operating Overhead:	**$1,450,000**
<u>Property Taxes and Insurances</u>	
Property Taxes and Insurance	
<u>Other Annual Expenses</u>	
Rental Fees (Office and Laboratory Space)	
Licensing Fees	
Miscellaneous	
Total Other Annual Expenses:	**$6,860,000**
Total Fixed Costs:	**$25,700,000**

18.5: Cash Flow Summary

Cash Flow Summary (' 000)

Year	Prod. Capacity	Price	Sales	Capital Cost	Working Capital	Var Cost	Fixed Cost	Depreciation (5 yr MACRS)	Depletion Allowance	Taxable Income	Taxes	Net Earnings	Cash Flow	Discounted Cash Flow	Cumulative NPV 15%
2022	0			(30,000)											
2023	0.45	4	54,000.00		(3,400)	(32,700)	(11,600)	(17,200)		(7,400)		(7,400)	6,400	5,600	**(31,100)**
2024	0.675	4	81,000.00		(3,400)	(49,000)	(17,300)	(27,400)		(12,800)		(12,800)	11,300	8,500	**(22,600)**
2025	0.9	4	108,000.00			(65,400)	(23,100)	(16,500)		3,000	1,200	1,800	18,300	12,000	**(10,600)**
2026	0.9	4	108,000.00			(65,400)	(23,100)	(9,900)		9,600	3,800	5,800	15,700	9,000	**(1,600)**
2027	0.9	4	108,000.00			(65,400)	(23,100)	(9,900)		9,600	3,800	5,800	15,700	7,800	**6,100**
2028	0.9	4	108,000.00			(65,400)	(23,100)	(4,900)		14,600	5,800	8,700	13,700	5,900	**12,100**
2029	0.9	4	108,000.00			(65,400)	(23,100)			19,500	7,800	11,700	11,700	4,400	**16,500**
2030	0.9	4	108,000.00			(65,400)	(23,100)			19,500	7,800	11,700	11,700	3,800	**20,300**
2031	0.9	4	108,000.00			(65,400)	(23,100)			19,500	7,800	11,700	11,700	3,300	**23,600**
2032	0.9	4	108,000.00			(65,400)	(23,100)			19,500	7,800	11,700	11,700	2,900	**26,500**
2033	0.9	4	108,000.00			(65,400)	(23,100)			19,500	7,800	11,700	11,700	2,500	**29,000**
2034	0.9	4	108,000.00			(65,400)	(23,100)			19,500	7,800	11,700	11,700	2,200	**31,200**
2035	0.9	4	108,000.00			(65,400)	(23,100)			19,500	7,800	11,700	11,700	1,900	**33,100**
2036	0.9	4	108,000.00			(65,400)	(23,100)			19,500	7,800	11,700	11,700	1,700	**34,800**
2037	0.9	4	108,000.00		13,400	(65,400)	(23,100)			19,500	7,800	11,700	25,100	3,100	**37,900**

18.6: Profitability Measures

Profitability Measures		
The Internal Rate of Return (IRR) for this project is		32.65%
The Net Present Value (NPV) of this project in 2023 is		$38,000,000
ROI Analysis (Third Production Year)		
Annual Sales	$108,000,000	
Annual Costs	$(88,500,000)	
Depreciation	$(6,125,000)	
Income Tax	$(7,800,000)	
Net Earnings	$11,700,000	
Total Capital Investment	$110,500,000	
ROI	10.6%	

18.7: Sensitivity Analysis

Price	**Variable Costs**				
	36300000	54500000	72600000	90800000	109000000
2	Negative IRR	Negative IRR	Negative IRR	Negative IRR	Negative IRR
3	48.28%	Negative IRR	Negative IRR	Negative IRR	Negative IRR
4	75.00%	71.18%	32.65%	0.88%	Negative IRR
5	97.06%	81.58%	65.31%	46.06%	21.60%
6	116.14%	101.97%	87.41%	72.27%	56.24%

Price	**Fixed Costs**				
	12800000	19300000	25700000	32100000	38500000
2	Negative IRR	Negative IRR	Negative IRR	Negative IRR	Negative IRR
3	3.49%	Negative IRR	Negative IRR	Negative IRR	Negative IRR
4	50.29%	41.55%	32.65%	23.03%	11.94%
5	76.92%	74.47%	65.31%	59.28%	52.79%
6	97.76%	92.62%	87.41%	82.13%	76.77%

Section 19: Other Important Considerations

19.1: Location

As previously mentioned in this report, China and India are the leading producers for numerous pharmaceuticals and relevantly, acetaminophen. The US represents the current leading consumer with urbanizing countries driving much of the new demand. For these reasons China and India were considered above the US to reduce costs related to capital investment, however, the plant was still designed to be in-line with the sufficient quality manufacturing practices to ensure compliance with standards of GMP. Recognizing the language barrier and utility needs, India was selected over China.

19.2: Environmental and Social Implications

The batch and continuous processes both produce acetaminophen powder and use para-aminophenol powder as a reagent. The batch process also involves seeding crystallization with acetaminophen crystals. Dust and powders are environmental hazards, therefore appropriate care needs to be applied in order to keep the powder contained. Appropriate personal protective equipment will be given to the employees to prevent inhalation of powders. It is recommended to pursue the use of utilities and heating agents that have the lowest environmental impact. This was not considered part of the project, but as the technologies used are not net-negative emission operations, a sensitivity on impact limitation should be conducted. It is important to recognize that while continuous does show to have fewer emissions (via utility and energy requirements), there are ways to reduce this further.

19.3 Shipping

To make sure that there is enough inventory to ensure that production is uninterrupted in the case of supplier mishaps, each facility's inventory should make up two shipments of reagents with one shipment in the warehouse and one en route to the facility. Para-aminophenol will be delivered in supersacks in shipping containers sourced from China and India. To ensure cleanliness standards, supersacks will be lined. Shipping containers are 8 ft wide, 8.5 ft tall, and 40 ft long. The supersacks are 45 in wide and long, and 48 in tall. With these dimensions, 20 supersacks could fit in each container. Each supersack can hold 1800 kg of p-aminophenol, and each month the continuous plant will need 915,000 kg of p-aminophenol per month, and 1,031,000 kg for the batch plant. This equates to 509 and 573 supersacks per month for the continuous and batch plants respectively. Acetic anhydride will be delivered in bulk fluid trucks sourced from India, where the plant is located. The prices used for reagents were global prices, the supply of these reagents from local sources would probably result in lower costs.

For the batch facility, an initial shipment of acetaminophen of 1.9 metric tons, enough for two cycles, will be delivered to the facility to conduct seeding before commencing operation of which a small portion will be set aside for seeding.

The acetaminophen powder will be shipped from the facility twice per month. The powder will be packed in lined supersacks through trucks, then to various buyers using shipping containers.

19.4 Cleaning

In order to maintain excellent product quality and output, the equipment for both processes need to be regularly cleaned. Clearly, increasing runtime between cleaning would increase to larger product quantities, and thus profits, but buildup in the equipment may reduce product quality, and output overtime. The runtime between cleaning sessions needs to be long enough to ensure that both the plants reach the production goal.

Section 20: Conclusions and Recommendations

An innovative and original continuous manufacturing process for acetaminophen powder was compared to the industry standard batch manufacturing train. Both plants were modeled under the same thermodynamic constraints and calibrated in SuperPro Designer leading to a financial comparative analysis as the foundation for new investment.

At a price of $4/kg, the continuous process will see a 15-year NPV of $38,000,000 with an IRR of 33% compared to $7,300,000 and 18% for batch. Sensitivity analyses demonstrate that continuous remains a more profitable investment across all tested variables. Fixed costs were used as proxy to plant scale to reach an understanding of what production conditions may prefer batch to continuous. While the difference between batch and continuous IRR appeared to converge, it was found that even a 50% reduction showed continuous to be 10% more profitable. Extending past profits, a holistic comparison reveals that not only are capital investment costs reduced with the continuous design, but energy requirements are lower, control over reaction profile and temperature is greater, and the ability to be flexible to volatile demand is superior.

To elute some of the major cost differences, the continuous process does not require intermediary storage vessels that correct for differences in batch process flow rates. Where the continuous in-line heat exchangers total to $88,000, the additional storage vessels that agitate and heat/cool the solution, total to $14,300,000 in the batch process. Further, the batch reactor and filter costs total to $35,200,000 compared to $29,900,000 for the continuous process. The 20% difference is attributed to more efficient heat transfer leading to less equipment and smaller reactors in the continuous scheme. Recognizing the increased number of process units, the batch process requires 36 pumps compared to the 30 of continuous, costing an additional $1,432,000.

Importantly, continuous also sees significant operation benefits. With fewer moving parts, the plant can run for a larger portion of the year and requires less maintenance. Additionally, the process sections require 2/3rd's the number of operators compared to batch. Combined, these benefits attribute to just over $2,000,000 in annual cost savings.

It is recommended that future analysis gain true understanding of activated carbon needs and composition. Pilot scale tests should be performed to understand the degree of variability to the theoretical model. Additionally, the pilot scale should include polymorph sensors and examine purity. While non-corrosive and stringent cleaning processes were implemented in design, recycling is not a favored practice amongst the pharmaceutical industry. Thus, confirmation of a non-contaminating process is vital for plant success. There is potential for a new optimization to be conducted on how an integration of batch, semi-batch and continuous could lead to maximized profits. For example, this project found that while batch reactors and filters were more expensive than continuous, the batch crystallizers, priced as autoclaves, were less expensive than the continuous MSMPR's which would suggest that a combination could be even more lucrative. Additionally, large scale continuous reactors are only of recent development and the conceptual economies of scale correlations used in this report may be underestimating plant-sized equipment.

This project has the potential to shape and inform future pharmaceutical investments as the irrefutable profitability of a continuous process is demonstrated for one of the most demanded OTC drugs on the market. Recognizing the rapidly growing demand for medicines, it is possible that the sale price was conservative where a $1/kg increase would see profits on the order of $126,000,000. It is highly recommended that continued development of this process be funded as the impact on society, pharmacy and the environment could be profound.

Section 21: Acknowledgements

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Section 22: Bibliography

[1] Future Market Insights Global and Consulting Pvt. Ltd. (2022, March 7). *Acetaminophen market to be worth US$ 14.07 billion by the year 2031 - Comprehensive Research Report by FMI*. GlobeNewswire News Room. Retrieved from https://www.globenewswire.com/newsrelease/2022/03/07/2397513/0/en/Acetaminophen-Market-to-be-worth-US-14-07-Billion-by-the-year-2031-Comprehensive-Research-Report-by-FMI.html#:~:text=According%20to%20a%20recent%20study,the%20forecast%20period%202021%2D2031

[2] *Acetaminophen PEP Review 99-15*. IHS Markit. (2002, December). Retrieved, from https://ihsmarkit.com/products/chemical-technology-pep-reviews-acetaminophen-2002.html

[3] *Paracetamol consumption market share, size, Trends & analysis by type, region insights, key players, applications and forecast to 2028*. Paracetamol Consumption Market Size, Global Forecast to 2028. (2020, April). Retrieved from https://www.eternityinsights.com/report/paracetamol-consumption-market

[4] ltd, R. and M. (2022, January). *Paracetamol market - growth, trends, COVID-19 impact, and forecasts (2022 - 2027)*. Research and Markets - Market Research Reports - Welcome. Retrieved April 17, 2022, from https://www.researchandmarkets.com/reports/4997604/paracetamol-market-growth-trends-covid-19

[5] Roberts, G. (2021, December 13). *Pharmaceutical market segmentation*. Orientation Marketing. Retrieved April 17, 2022, from https://www.orientation.agency/insights/pharmaceutical-market-segmentation

[6] Letter, T. P. (1994, June 26). *The changing US analgesia market*. TPL. Retrieved April 17, 2022, from https://www.thepharmaletter.com/article/the-changing-us-analgesia-market

[7] *Analgesics: Uses, treatment, risks*. Cleveland Clinic. (2021, March). Retrieved April 17, 2022, from https://my.clevelandclinic.org/health/drugs/21483-analgesics

[8] project statement

[9] *Continuous vs. batch production - contract pharma*. (2018, October). Retrieved April 18, 2022, from https://www.contractpharma.com/issues/2018-04-01/view_features/continuous-vs-batch-production

[10] *Pharmaceuticals & Healthcareindustry Research*. Pharma & Healthcare Industry Analysis :: Fitch Solutions. (2021, October). Retrieved from https://www.fitchsolutions.com/pharma-healthcare

[11] Research and Markets. (2021, October 7). *Worldwide paracetamol industry to 2026 - cold and cough segment is dominating The paracetamol market*. GlobeNewswire News Room. Retrieved from https://www.globenewswire.com/news-release/2021/10/07/2310078/28124/en/Worldwide-Paracetamol-Industry-to-2026-Cold-and-Cough-Segment-is-Dominating-the-Paracetamol-Market.html

[12] *Global acetaminophen (paracetamol) market – industry trends and forecast to 2028*. Acetaminophen (Paracetamol) Market – Global Industry Trends and Forecast to 2028 | Data Bridge Market Research. (n.d.). Retrieved from https://www.databridgemarketresearch.com/reports/global-acetaminophen-paracetamol-

market#:~:text=Acetaminophen%20is%20also%20commonly%20known,for%20mild%20to%20moderate%20pain
[13] *Acetaminophen market*. Future Market Insights | Market Research and Consulting Company. (2022, February)., from https://www.futuremarketinsights.com/reports/acetaminophen-market
[14] Mohammed, M., Syed, M. F., Bhatt, M. J., Hoffman, E. J., & Aslan, K. (2012, April 4). *Rapid and selective crystallization of acetaminophen using metal-assisted and microwave-accelerated evaporative crystallization*. Nano biomedicine and engineering. Retrieved, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3319136/
[15] 15 Knapp, B. S., By: & Knapp, S. (2020, October 28). *Acetic acid - the definitive guide*. Biology Dictionary. Retrieved April 16, 2022, from https://biologydictionary.net/acetic-acid/
[16] Office, E. P. (2009, October). *Global patent index - EP 2266949 A1*. EP 2266949 A1 20101229 - "Fast, high-efficiency quantitative synthesis of paracetamol". Retrieved April 18, 2022, from https://data.epo.org/gpi/EP2266949A1-quot-Fast-high-efficiency-quantitative-synthesis-of-paracetamol-quot
[17] U.S. National Library of Medicine. (n.d.). *Acetic anhydride*. National Center for Biotechnology Information. PubChem Compound Database. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Acetic-anhydride
[18] U.S. National Library of Medicine. (n.d.). *4-aminophenol*. National Center for Biotechnology Information. PubChem Compound Database. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/403
[19] U.S. National Library of Medicine. (n.d.). *Water*. National Center for Biotechnology Information. PubChem Compound Database. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/962
[20] U.S. National Library of Medicine. (n.d.). *Acetic acid*. National Center for Biotechnology Information. PubChem Compound Database. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/176
[21] Synthesis of p-Aminophenol by Catalytic Hydrogenation of Nitrobenzene, C. V. Rode, M. J. Vaidya, and R. V. Chaudhari; *Organic Process Research & Development* **1999** *3* (6), 465-470; DOI: 10.1021/op990040r
[22] U.S. National Library of Medicine. (n.d.). *Ammonium chloride*. National Center for Biotechnology Information. PubChem Compound Database. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Ammonium-chloride
[23] Centers for Disease Control and Prevention. (2018, April 4). *CDC*. Centers for Disease Control and Prevention. Retrieved April 18, 2022, from https://emergency.cdc.gov/agent/benzene/basics/facts.asp
[24] Libretexts. (2020, July 26). *2: Synthesis of acetaminophen (experiment)*. Chemistry LibreTexts. Retrieved April 18, 2022, from https://chem.libretexts.org/Ancillary_Materials/Laboratory_Experiments/Wet_Lab_Experiments/Organic_Chemistry_Labs/Experiments/2%3A__Synthesis_of_Acetaminophen_(Experiment)
[25] *Synthesis of acetaminophen* . Acetaminophen . (2006). Retrieved from http://rene.souty.free.fr/IMG/pdf/ParacetamolProtocolFLORIDacetaminophen.pdf
[26] “Manufacturing & Effluent Treatment Process” Adroit Pharmaceuticals Pvt.Ltd. Amadi (V), Nagpur **(D).**
[27] Wikimedia Foundation. (2022, February 28). *Acetic acid (data page)*. Wikipedia. Retrieved April 18, 2022, from https://en.wikipedia.org/wiki/Acetic_acid_(data_page)

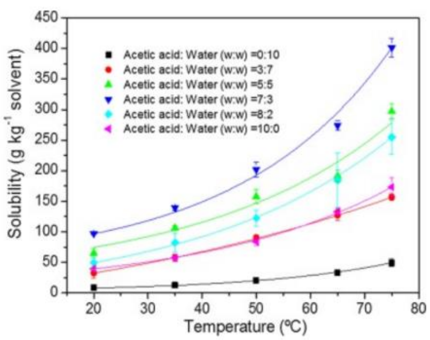
[28] *Water - specific heat vs. temperature*. Engineering ToolBox. (n.d.). Retrieved April 18, 2022, from https://www.engineeringtoolbox.com/specific-heat-capacity-water-d_660.html
[29] *Chemical properties of phenol, 4-amino- (CAS 123-30-8)*. Chemeo High Quality Chemical Properties. (n.d.). Retrieved April 18, 2022, from https://www.chemeo.com/cid/59-313-9/Phenol%2C%204-amino-
[30] National Institute of Standards and Technology. *Acetic anhydride*. NIST Chemistry WebBook. (n.d.). Retrieved April 18, 2022, from https://webbook.nist.gov/cgi/cbook.cgi?ID=C108247&Mask=1EFF
[31] National Institute of Standards and Technology. *Acetaminophen*. NIST Chemistry WebBook. (n.d.). Retrieved April 18, 2022, from https://webbook.nist.gov/cgi/cbook.cgi?ID=C103902&Mask=4
[32] Seider, W. D., Lewin, D. R., Seader, J. D., Widagdo, S., Gani, R., & Ng, K. M. (2017). *Product and process design principles: Synthesis, analysis, and evaluation*. John Wiley & Sons Inc.
[33] *Aminophenol*. Alibaba.com. (n.d.). Retrieved April 18, 2022, from https://www.alibaba.com/showroom/aminophenol.html
[34] Jiang, M., & Ni, X.-W. (2018). Effects of water and temperature on reaction mechanism and crystal properties in a reactive crystallization of Paracetamol. *Chemical Engineering and Processing - Process Intensification*, *131*, 20–26. https://doi.org/10.1016/j.cep.2018.07.006
[35] Hirota, W. H., Rodrigues, R. B., Sayer, C., & Giudici, R. (2010). Hydrolysis of acetic anhydride: Non-adiabatic calorimetric determination of kinetics and Heat Exchange. *Chemical Engineering Science*, *65*(12), 3849–3858. https://doi.org/10.1016/j.ces.2010.03.028
[36] Jiang, M., & Ni, X.-W. (2019). Effects of solvents and impurity on crystallization kinetics and crystal properties in a reactive crystallization of Paracetamol. *Journal of Crystal Growth*, *523*, 125150. https://doi.org/10.1016/j.jcrysgro.2019.125150
[37] Granberg, R. A., & Rasmuson, Å. C. (1999). Solubility of paracetamol in pure solvents. *Journal of Chemical & Engineering Data*, *44*(6), 1391–1395. https://doi.org/10.1021/je990124v
[38] Jiang, M., & Ni, X.-W. (2019). Reactive crystallization of paracetamol in a continuous oscillatory baffled reactor. *Organic Process Research & Development*, *23*(5), 882–890. https://doi.org/10.1021/acs.oprd.8b00446
[39] *Sodium Chloride Water Solutions*. Engineering ToolBox. (n.d.). Retrieved April 18, 2022, from https://www.engineeringtoolbox.com/sodium-chloride-water-d_1187.html
[40] Carpenter, K. J. (2011, February 25). *Agitated vessel heat transfer*. THERMOPEDIA. Retrieved April 18, 2022, from https://thermopedia.com/content/547/
[41] *Metals, metallic elements and alloys - thermal conductivities*. Engineering ToolBox. (n.d.). Retrieved April 18, 2022, from https://www.engineeringtoolbox.com/thermal-conductivity-metals-d_858.html
[42] *Metals, metallic elements and alloys - thermal conductivities*. Engineering ToolBox. (n.d.). Retrieved April 18, 2022, from https://www.engineeringtoolbox.com/thermal-conductivity-metals-d_858.html
[43] *Metals, metallic elements and alloys - thermal conductivities*. Engineering ToolBox. (n.d.). Retrieved April 18, 2022, from https://www.engineeringtoolbox.com/thermal-conductivity-metals-d_858.html

[44] *The properties of glass lining*. Glass Lining Technologies - Bart Company. (n.d.). Retrieved April 18, 2022, from http://www.bartcompany.com/wp-content/uploads/PDF/duker/TE_Email_Technik_E_Stand_04_09.pdf
[45] Wikimedia Foundation. (2022, April 12). *Paracetamol*. Wikipedia. Retrieved April 18, 2022, from https://en.wikipedia.org/wiki/Paracetamol
[46] Wikimedia Foundation. (2022, April 4). *Acetic acid*. Wikipedia. Retrieved April 18, 2022, from https://en.wikipedia.org/wiki/Acetic_acid
[47] *What Is Activated Carbon?* TIGG LLC Activated Carbon Equipment Media and Services. (n.d.). Retrieved April 18, 2022, from https://tigg.com/resources/activated-carbon-knowledge-base/what-is-activated-carbon/

Section 23: Appendix

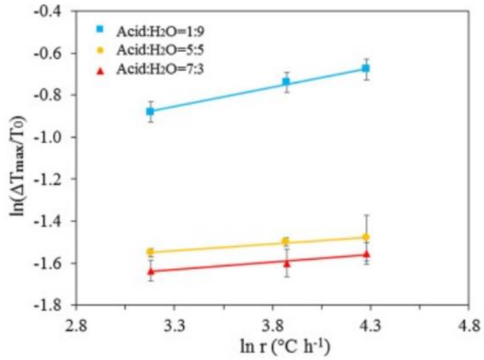
A.1: Reaction composition

Figure A.1: Solubility



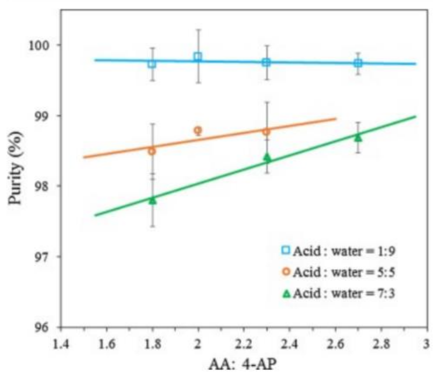
Solubility of paracetamol in different ratios of acetic acid to water

Figure A.2: Nucleation rate



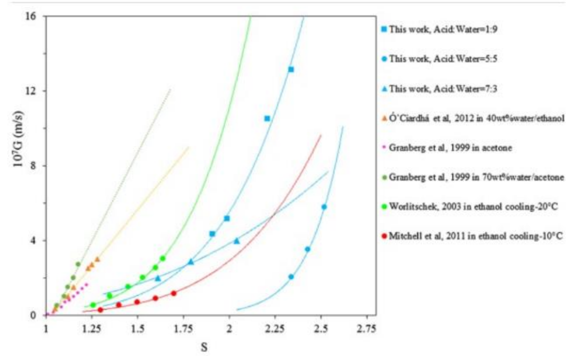
The MSZW increases for each solvent system showing that increased solubility increase nucleation rate

Figure A.3: Purity

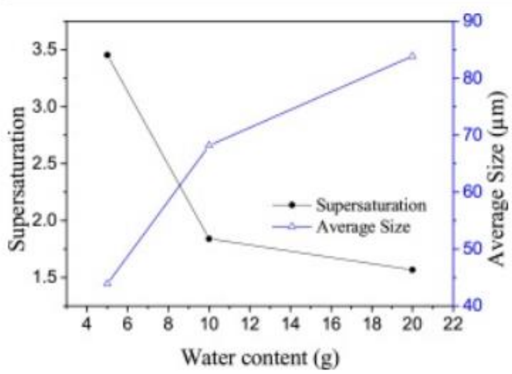


High purities for all solvents

Figure A.4: Solubility



Comparison of growth rates between Jiang et al and other work show no direct dependence of crystal growth order on the solvent composition



The supersaturation and crystal size as a function of water contents

Prior to commencing any process synthesis, multiple lab scale reports were gathered to get an understanding of reaction composition. Initially, the reports would use a 1:1 ratio of reactants which would lead to a yield around 70% as demonstrated by ChemLibreTexts using 2.1g of p-aminophenol and 2.0mL of acetic anhydride. This composition was corroborated with another experiment who used 0.150g of p-aminophenol and 0.165mL acetic anhydride and obtained 65% yield. Recognizing that this was the reaction pathway the project would follow, the next step was to obtain kinetics data. As outlined in Section 9, a range of kinetic values were given for different solvent compositions. It was thus important to make a sound decision on which composition to use. Presented in the five figures above, Figures A.1, A.2, A.3, A.4 and A.5, solvent composition impacts solubility, nucleation orders, growth rates and purity.

To obtain the best yield, the largest difference in solubility across the temperature range of the reaction is desired to elute the most crystals. There is no direct pattern for how increasing or decreasing the ratio of Acid:H2O impacted solubility thus optimizing the other variables was the next priority. Jiang et al found that a higher ratio of Acid:H2O at the end of reaction leads to a higher nucleation order. The ratio did not have a clear impact on the growth rates but those presented are comparable to other recrystallisation data. Additionally, project consultants advised that smaller crystals are better for downstream processes. Overall, this demonstrated that the larger the solvent ratio, the most overall benefit. Plotting the curves on excel and run an iterative analysis revealed that an 8:2 ratio would result in the most crystal yield.

The 8:2 ratio then supported a follow-on study from Jiang et al who determined pseudo first-order kinetics by using an excess of acetic anhydride. As the end composition was now known, it was possible to back calculate the necessary starting reagents.

A.2: Vacuum

Starting from a batch size 50264 kg (7:3 weight ratio of acetaminophen to water), 20 mols, or approximately 600 kg, of material were vacuumed out in steps. After each step the necessary pressure and weight ratios were calculated. Repeating this process, it is seen that for significant energy needs, the composition changes marginally. Acetic Acid composition goes from 0.558 to 0.552 after enough energy is expended that the extra yield was no longer economical. This reality is attributed to the similar boiling points and thus this proposal was rejected

				Removed		Ratios		Acetic acid					Water				
Step	Temperature (K)	joules	Pressure	kg	mol	kg	mol	Molar mass (g/mol)	Heat of vap (j/mol)	kg	mol	Cp (J/molK)	Molar mass (g/mol)	Heat of vap	kg	mol	Cp (J/mol K)
0	339					0.3	0.588	60.05	40000	35184.0	585.9	63.4	18.015	40000	15079.2	837.0	75.9
0.5	-7.9460	800000	0.217	604.103	20	0.423	0.71	60.05	40000	348.29	5.8	63.4	18.015	40000	255.813	14.2	75.9
1	331.05					0.298	0.586	60.05	40000	34836.0	580.1	63.4	18.015	40000	14823.4	822.8	75.9
1.5	-8.0618	800000	0.1508	612.51	20	0.411	0.7	60.05	40000	360.3	6	63.4	18.015	40000	252.21	14	75.9
2	322.99					0.297	0.584	60.05	40000	34476.	574.1	63.4	18.015	40000	14571.1	808.8	75.9
2.5	-8.1807	800000	0.097	614.10733	20	0.409	0.698	60.05	40000	362.	6.038	63.4	18.015	40000	251.525	13.96	75.9
3	314.81					0.295	0.566	60.05	40000	34113.	568.0	63.4	18.015	40000	14319.6	794.8	75.9
3.5	-8.3032	800000	0.065	624.2798	20	0.395	0.686	60.05	40000	377.1	6.28	63.4	18.015	40000	247.168	13.72	75.9
4	306.50					0.254	0.581	60.05	40000	33736.5	561.8	63.4	18.015	40000	14072.5	781.1	75.9
								60.05	40000	0	0	63.4	18.015	40000	0	0	75.9

A.3: Solubility

The researchers already fit an exponential curve to the data points they found, the goal for future calculation was to replicate that exponential curve. First, the vertical scale was measured using a vertical line from 0 to 450 and the length was set as 450 to be the scale of the image. This way, any vertical line from the x-axis will read the solubility. Then, measuring vertically up to the solubility curve from 20-75 C in intervals of 5 C created the data points the line should fit. The temperature was converted to Kelvins. In excel, an exponential correlation function was also specified in the form of Solubility=a*e^(b*Temp)+c with a, b, and c as unknown variables. The square difference between the measured solubility and the correlation solubility was calculated. Using the Solver function, the square difference was minimized while the variables a, b, and c were allowed to change. The variables were a=0.008161104, b=0.029753937, and c=0, combining everything, the solubility function in g acetaminophen/kg solvent becomes 0.001501*EXP(0.0355626*TEMP)+46.06541. As acetic acid is much more expensive than water, this identical analysis was performed on the 8:2 and 5:5 acetic acid: water ratios. The equations were found to be 0.008161104*EXP(0.029753937*TEMP)+0 and 0.01554*EXP(0.027955*TEMP)+17.01735 respectively. With this equation, the amount of dissolved acetaminophen at any given temperature can be determined. More importantly, this also gives information on the amount of crystalized acetaminophen as the total amount minus the dissolved amount.

A.4: Reaction Profile

Batch Time

Reaction and Crystallization Properties

RXN 1		
A	11,292.93	1/s
-delH	-37800	J/mol
E	37310	J/mol
ca0	1.91010535	mol/L
RXN 2		
A	8103.083928	1/s
-delH	58900	J/mol
E	43000	J/mol
RXN multiplier	2.8	
ca0	5.348294979	mol/L
Temp Control		
X1 cutoff	0.9	
U	100	W/m2K
Area	55.8136515	m2
Crystallzation	27600	J/mol
Max Temp	352.721	K
Max time (Calc)	2,240	s
Max time (Hard paste)	2240	s
Acetaminophen MW	151.16	g/mol
Solvent mass	35165.42895	kg
Vr	34346.04031	L
R	8.314462618	J/Kmol
cp	2.191963896	J/gK
rho	1342.132237	g/L

Select Time Points for Reaction and Crystallization Pathway

Time	Temperature	Reaction 1	Reaction 2	Cooling	Crystalization	Change in Temperature
min	K	Fraction of Conversion	Fraction of Conversion	J/s	J/s	K/s
0	319.00	0.0000	0.0000	0.00E+00		-1.37E-01
1	313.36	0.3850	0.1730	0.00E+00	0	-5.41E-02
2	310.98	0.5883	0.2700	0.00E+00	0	-2.38E-02
3	309.99	0.7155	0.3353	0.00E+00	0	-7.98E-03
4	309.77	0.8012	0.3836	0.00E+00	0	1.85E-03
5	310.07	0.8611	0.4214	0.00E+00	0	8.67E-03
6	310.72	0.9037	0.4525	-3.49E+05	0	1.03E-02
7	311.44	0.9340	0.4790	-3.53E+05	0	1.42E-02
8	312.37	0.9555	0.5022	-3.59E+05	0	1.72E-02
9	313.47	0.9706	0.5233	-3.65E+05	0	1.97E-02
10	314.70	0.9810	0.5430	-3.72E+05	0	2.19E-02
12	317.53	0.9927	0.5805	-3.87E+05	0	2.54E-02
14	320.75	0.9976	0.6178	-4.05E+05	0	2.84E-02
16	324.30	0.9993	0.6566	-4.25E+05	0	3.10E-02
18	328.14	0.9999	0.6976	-4.47E+05	0	3.30E-02
20	332.18	1	0.7405	-4.69E+05	0	3.43E-02
30	349.61	1	0.9322	-5.67E+05	0	1.65E-02
37.3	352.72	1	0.9848	-5.84E+05	0	-1.19E-04
40	352.57	1	0.9913	-5.83E+05	88,813	-1.69E-03
50	350.85	1	0.9989	-5.74E+05	184,232	-3.47E-03
60	348.69	1	0.9998	-5.62E+05	184,050	-3.68E-03
90	342.03	1	1	-5.24E+05	151,395	-3.69E-03
120	335.44	1	1	-4.88E+05	122,014	-3.62E-03
150	329.03	1	1	-4.52E+05	98,192	-3.50E-03
180	322.86	1	1	-4.17E+05	78,340	-3.35E-03
240	311.39	1	1	-3.53E+05	49,847	-3.00E-03
300	301.27	1	1	-2.97E+05	32,142	-2.62E-03
330	296.73	1	1	-2.72E+05	26,024	-2.42E-03

360	292.52	1	1	-2.47E+05	21,207	-2.24E-03
396	287.91	1	1	0.00E+00	16,736	-2.03E-03

Note, this analysis was performed using a time step of 10 seconds to ensure the reaction profile was accurate. Presented above is a condensed form in minutes for the readers benefit. At 37.3 minutes is when the maximum temperature was reached and crystallization energy was included. At 396 minutes is when the temperature first drops below 288 K and the cooling process is complete.

Recrystallization Properties

Crystallization	27600	J/mol
Max Temp	352.721	K
Max time (Calc)	2,240	s
Max time (Hard paste)	2240	s
Acetaminophen MW	151.16	g/mol
Solvent mass	35534.33258	kg
Vr	34706.34813	L
R	8.314462618	J/Kmol
cp	2.19206407	J/gK
rho	1341.961158	g/L

Select Time Points for Recrystallization Pathway

Time	Temp	Cooling	Crystallization	Change in Temp
hours	K	J/s	J/s	K/s
0.0	353.0000	-5.89E+05	0.00E+00	-5.77E-03
0.5	345.9800	-5.50E+05	1.70E+05	-3.72E-03
1.0	339.3800	-5.13E+05	1.42E+05	-3.63E-03
1.5	332.9000	-4.76E+05	1.14E+05	-3.55E-03
2.0	326.6	-4.41E+05	9.15E+04	-3.42E-03
2.5	320.55	-4.07E+05	7.31E+04	-3.27E-03
3.0	314.8	-3.74E+05	5.84E+04	-3.10E-03
3.5	309.36	-3.44E+05	4.67E+04	-2.91E-03

4.0	304.26	-3.15E+05	3.75E+04	-2.72E-03
4.5	299.51	-2.88E+05	3.03E+04	-2.53E-03
5.0	295.1	-2.64E+05	2.46E+04	-2.34E-03
5.5	291.02	-2.41E+05	2.01E+04	-2.16E-03
5.92	287.87	-2.23E+05	1.70E+04	-2.02E-03

Note, this analysis was performed using a time step of 5 minutes to ensure the cooling rate is accurate.

Energy and Utility Requirements

Cooling Agent	**CaCl2 Brine**	
T in	243	K
T out	253	K
Heat Capacity	2.7	J/g*K
Cost	0.25	$/MT
Reaction and Crystallization		
Time	396	min
Cooling agent	-9.22E+09	J
	3.41E+05	kg
	85.35	$
Max cooling agent	-5.84E+05	J/s
	21.63	kg/s
	342.9	gal/min
Recrystallization		
Time	355	min
Cooling agent	-8.30E+09	J
	3.07E+05	kg
	76.81	$

Heating Agent	**5 atm Steam**	
T in	425.00	K
T out	425.00	K
U	310.00	W/m2K
Condensation	2,107.40	kJ/kg
Cost	12.00	$/MT
Preheating Water+Recycle1		
Mass	19,708.66	kg
Heat capacity	3.03	J/gK
T in	292.69	K
T out	319.00	K
Time	90.00	min

Cooling Agent	**Chilled Water**	
T in	278	K
T out	283	K
U	100	W/m2K
Heat Capacity	4.18	J/gK
Cost	0.40	$/MT
Filter 1, 8:2 Wash		
Mass	4,710	kg
Heat capacity	2.48	J/gK
T in	349.1	K
T out	288	K
Time	30	min

Area	7.92	m2
Agent Required	746.43	kg
Cost	8.96	$
Preheating Acetic Anhydride		
Mass	18,753.19	kg/cycle
Heat capacity	1.65	J/gK
T in	298.00	K
T out	319.00	K
Time	90.00	min
Area	3.34	m2
Agent Required	307.89	kg
Cost	3.69	$
Preheating Solvent		
Mass	35,916.16	kg/cycle
Heat capacity	2.44	J/gK
T in	303.04	K
T out	353.00	K
Time	90.00	min
Area	27.64	m2
Agent Required	2,081.21	kg
Cost	24.97	$

Area	133.65	m2
Agent Required	34,174	kg
Cost	13.67	$
Filter 1, Water Wash		
Mass	4,710	kg
Heat capacity	4.21	J/gK
T in	298	K
T out	288	K
Time	30	min
Area	89.39	m2
Agent Required	9,485	kg
Cost	3.79	$
Filter 2, 8:2 Wash		
Mass	4,756	kg
Heat capacity	2.48	J/gK
T in	349.1	K
T out	288	K
Time	30	min
Area	134.98	m2
Agent Required	34,514	kg
Cost	13.81	$
Filter 2, Water Wash		
Mass	4,756	kg
Heat capacity	4.21	J/gK
T in	298	K
T out	288	K
Time	30	min
Area	90.28	m2
Agent Required	9,579	kg
Cost	3.83	$

CSTR Time

Properties Used

Reaction 1			Reaction 2					
A	11293	1/s	A	8103	1/s	rho	1000	g/L
-delH	-37800	J/mol	-delH	58900	J/mol	R	8.314	J/Kmol
E	37310	J/mol	E	43000	J/mol			

CSTR reaction calculation

				1 CSTR		2 CSTR		3 CSTR		4 CSTR		5 CSTR	
Temperature	Total Time	k1	k2	Reaction 1	Reaction 2	Reaction 1	Reaction 2	Reaction 1	Reaction 2	Reaction 1	Reaction 2	Reaction 1	Reaction 2
K	s	1/s	1/s	Fraction	Fraction	Fraction	Fraction	Fraction	Fraction	Fraction	Fraction	Fraction	Fraction
353	60	3.40E-02	3.51E-03	0.67133	0.17416	0.75524	0.18168	0.78942	0.18438	0.80798	0.18578	0.81962	0.18663
353	120	3.40E-02	3.51E-03	0.80335	0.29666	0.89198	0.31800	0.92409	0.32609	0.94009	0.33035	0.94951	0.33298
353	180	3.40E-02	3.51E-03	0.85970	0.38751	0.93945	0.42289	0.96450	0.43678	0.97567	0.44421	0.98168	0.44885
353	240	3.40E-02	3.51E-03	0.89095	0.45758	0.96133	0.50531	0.98063	0.52449	0.98833	0.53487	0.99211	0.54138
353	300	3.40E-02	3.51E-03	0.91082	0.51326	0.97318	0.57127	0.98829	0.59490	0.99373	0.60777	0.99616	0.61588
353	360	3.40E-02	3.51E-03	0.92456	0.55857	0.98032	0.62486	0.99240	0.65207	0.99633	0.66694	0.99796	0.67632
353	420	3.40E-02	3.51E-03	0.93463	0.59617	0.98494	0.66900	0.99478	0.69897	0.99772	0.71536	0.99883	0.72570
353	480	3.40E-02	3.51E-03	0.94233	0.62786	0.98811	0.70578	0.99627	0.73780	0.99850	0.75529	0.99929	0.76631
353	540	3.40E-02	3.51E-03	0.94841	0.65494	0.99037	0.73675	0.99724	0.77023	0.99898	0.78845	0.99955	0.79991
353	600	3.40E-02	3.51E-03	0.95333	0.67835	0.99205	0.76308	0.99790	0.79753	0.99928	0.81619	0.99971	0.82788
353	660	3.40E-02	3.51E-03	0.95739	0.69878	0.99332	0.78565	0.99837	0.82066	0.99948	0.83952	0.99980	0.85129
353	720	3.40E-02	3.51E-03	0.96080	0.71677	0.99431	0.80514	0.99870	0.84041	0.99961	0.85927	0.99986	0.87098
353	780	3.40E-02	3.51E-03	0.96371	0.73274	0.99509	0.82209	0.99895	0.85735	0.99971	0.87607	0.99990	0.88762
353	840	3.40E-02	3.51E-03	0.96621	0.74700	0.99573	0.83692	0.99914	0.87199	0.99977	0.89044	0.99993	0.90175
353	900	3.40E-02	3.51E-03	0.96839	0.75981	0.99625	0.84997	0.99929	0.88468	0.99982	0.90278	0.99995	0.91380
353	960	3.40E-02	3.51E-03	0.97031	0.77139	0.99667	0.86151	0.99941	0.89575	0.99986	0.91343	0.99996	0.92412
353	1020	3.40E-02	3.51E-03	0.97201	0.78191	0.99703	0.87177	0.99950	0.90545	0.99989	0.92267	0.99997	0.93300
353	1080	3.40E-02	3.51E-03	0.97352	0.79150	0.99734	0.88093	0.99957	0.91398	0.99991	0.93070	0.99998	0.94065
353	1140	3.40E-02	3.51E-03	0.97488	0.80028	0.99760	0.88915	0.99963	0.92152	0.99992	0.93772	0.99998	0.94728
353	1200	3.40E-02	3.51E-03	0.97611	0.80835	0.99782	0.89654	0.99968	0.92820	0.99994	0.94387	0.99998	0.95304
353	1260	3.40E-02	3.51E-03	0.97722	0.81580	0.99802	0.90322	0.99972	0.93414	0.99995	0.94928	0.99999	0.95807
353	1320	3.40E-02	3.51E-03	0.97823	0.82269	0.99818	0.90927	0.99975	0.93945	0.99996	0.95405	0.99999	0.96246

353	1380	3.40E-02	3.51E-03	0.97916	0.82908	0.99833	0.91477	0.99978	0.94420	0.99996	0.95828	0.99999	0.96631
353	1440	3.40E-02	3.51E-03	0.98001	0.83502	0.99846	0.91978	0.99981	0.94846	0.99997	0.96203	0.99999	0.96969
353	1500	3.40E-02	3.51E-03	0.98079	0.84057	0.99858	0.92437	0.99983	0.95230	0.99997	0.96537	0.99999	0.97268
353	1560	3.40E-02	3.51E-03	0.98152	0.84576	0.99868	0.92857	0.99985	0.95577	0.99998	0.96835	1.00000	0.97532
353	1620	3.40E-02	3.51E-03	0.98219	0.85062	0.99878	0.93243	0.99986	0.95892	0.99998	0.97101	1.00000	0.97766
353	1680	3.40E-02	3.51E-03	0.98282	0.85518	0.99886	0.93599	0.99988	0.96177	0.99998	0.97340	1.00000	0.97974
353	1740	3.40E-02	3.51E-03	0.98340	0.85947	0.99893	0.93927	0.99989	0.96436	0.99998	0.97555	1.00000	0.98159
353	1800	3.40E-02	3.51E-03	0.98394	0.86352	0.99900	0.94231	0.99990	0.96672	0.99999	0.97749	1.00000	0.98324
353	1860	3.40E-02	3.51E-03	0.98445	0.86733	0.99906	0.94513	0.99991	0.96888	0.99999	0.97924	1.00000	0.98472
353	1920	3.40E-02	3.51E-03	0.98493	0.87095	0.99912	0.94774	0.99992	0.97086	0.99999	0.98082	1.00000	0.98604
353	1980	3.40E-02	3.51E-03	0.98538	0.87436	0.99917	0.95017	0.99992	0.97267	0.99999	0.98226	1.00000	0.98723
353	2040	3.40E-02	3.51E-03	0.98580	0.87761	0.99922	0.95244	0.99993	0.97433	0.99999	0.98356	1.00000	0.98830
353	2100	3.40E-02	3.51E-03	0.98620	0.88069	0.99926	0.95455	0.99993	0.97587	0.99999	0.98474	1.00000	0.98926
353	2160	3.40E-02	3.51E-03	0.98658	0.88362	0.99930	0.95653	0.99994	0.97728	0.99999	0.98582	1.00000	0.99013
353	2220	3.40E-02	3.51E-03	0.98694	0.88640	0.99934	0.95838	0.99994	0.97859	0.99999	0.98681	1.00000	0.99092
353	2280	3.40E-02	3.51E-03	0.98728	0.88906	0.99937	0.96011	0.99995	0.97979	0.99999	0.98771	1.00000	0.99163
353	2340	3.40E-02	3.51E-03	0.98760	0.89160	0.99940	0.96174	0.99995	0.98091	0.99999	0.98854	1.00000	0.99228
353	2400	3.40E-02	3.51E-03	0.98791	0.89402	0.99943	0.96327	0.99996	0.98195	1.00000	0.98930	1.00000	0.99286
353	2460	3.40E-02	3.51E-03	0.98820	0.89634	0.99946	0.96471	0.99996	0.98291	1.00000	0.98999	1.00000	0.99340
353	2520	3.40E-02	3.51E-03	0.98848	0.89856	0.99948	0.96607	0.99996	0.98381	1.00000	0.99063	1.00000	0.99388
353	2580	3.40E-02	3.51E-03	0.98874	0.90068	0.99950	0.96735	0.99996	0.98464	1.00000	0.99122	1.00000	0.99433
353	2640	3.40E-02	3.51E-03	0.98900	0.90272	0.99953	0.96856	0.99997	0.98542	1.00000	0.99177	1.00000	0.99474
353	2700	3.40E-02	3.51E-03	0.98924	0.90467	0.99955	0.96970	0.99997	0.98614	1.00000	0.99227	1.00000	0.99511
353	2760	3.40E-02	3.51E-03	0.98947	0.90655	0.99957	0.97079	0.99997	0.98682	1.00000	0.99274	1.00000	0.99545
353	2820	3.40E-02	3.51E-03	0.98969	0.90836	0.99958	0.97181	0.99997	0.98746	1.00000	0.99317	1.00000	0.99576
353	2880	3.40E-02	3.51E-03	0.98990	0.91010	0.99960	0.97278	0.99997	0.98805	1.00000	0.99357	1.00000	0.99605
353	2940	3.40E-02	3.51E-03	0.99011	0.91177	0.99962	0.97371	0.99998	0.98861	1.00000	0.99394	1.00000	0.99631
353	3000	3.40E-02	3.51E-03	0.99030	0.91338	0.99963	0.97458	0.99998	0.98913	1.00000	0.99428	1.00000	0.99656
353	3060	3.40E-02	3.51E-03	0.99049	0.91493	0.99965	0.97542	0.99998	0.98963	1.00000	0.99460	1.00000	0.99678
353	3120	3.40E-02	3.51E-03	0.99067	0.91643	0.99966	0.97621	0.99998	0.99009	1.00000	0.99490	1.00000	0.99699
353	3180	3.40E-02	3.51E-03	0.99085	0.91788	0.99967	0.97696	0.99998	0.99053	1.00000	0.99518	1.00000	0.99718
353	3240	3.40E-02	3.51E-03	0.99102	0.91928	0.99968	0.97768	0.99998	0.99094	1.00000	0.99543	1.00000	0.99736
353	3300	3.40E-02	3.51E-03	0.99118	0.92063	0.99969	0.97837	0.99998	0.99132	1.00000	0.99568	1.00000	0.99752
353	3360	3.40E-02	3.51E-03	0.99133	0.92194	0.99970	0.97903	0.99998	0.99169	1.00000	0.99590	1.00000	0.99767

353	3420	3.40E-02	3.51E-03	0.99148	0.92320	0.99971	0.97965	0.99998	0.99203	1.00000	0.99611	1.00000	0.99781
353	3480	3.40E-02	3.51E-03	0.99163	0.92443	0.99972	0.98025	0.99998	0.99236	1.00000	0.99631	1.00000	0.99794
353	3540	3.40E-02	3.51E-03	0.99177	0.92561	0.99973	0.98082	0.99999	0.99267	1.00000	0.99650	1.00000	0.99806
353	3600	3.40E-02	3.51E-03	0.99191	0.92676	0.99974	0.98137	0.99999	0.99296	1.00000	0.99667	1.00000	0.99818

CSTR Heating

Reactor

	RXN 1	RXN 2	
A	11293	8103	1/s
-delH	-37800	58900	J/mol
E	37310	43000	J/mol
All	5.6203	kg/s	
4-Aminophenol	1	kg/s	
Acetic anhydride	2.3115	kg/s	
rho	1328	g/L	
Cp	2.2017	J/gK	
R	8.3145	J/Kmol	
U	100	W/m2K	
Crystallization	27600	J/mol	
Solvent	4.332	kg/s	
Cooling Agent	NaCl		
T in	263	K	
T out	273	K	
Heat Capacity	3.45	J/g*K	
Cost	0.25	$/MT	

2	CSTR								
T	tau	volume	Qmax	Ca0,1	Ca0,2	Ca1,1	Ca1,2	Q1	T input
K	s	m3	J/s	mol/L	mol/L	mol/L	mol/L		K
353	2760	7.76	1.68E+05	1.9113	3.4404	0.0398	0.5880	-3.26E+05	326.66
						0.9792	0.8291		
3	CSTR								
T	tau	volume	Qmax	Ca0,1	Ca0,2	Ca1,1	Ca1,2	Q1	T input
353	1920	3.60	1.01E+05	1.9113	3.4404	0.0839	1.0587	-2.63E+05	331.72
						0.9561	0.6923		
4	CSTR								
T	tau	volume	Qmax	Ca0,1	Ca0,2	Ca1,1	Ca1,2	Q1	T input
353	1620	2.28	7.42E+04	1.9113	3.4404	0.1293	1.4196	-2.16E+05	335.57
						0.9324	0.5874		

2	CSTR	continued							
Ca2,1	Ca2,2	Q2							
mol/L	mol/L	J/s							
0.0008	0.1005	-6.51E+04							
0.9996	0.9708	1.89	kg/s						
		4.72E-04	$/s						
3	CSTR	continued							
Ca2,1	Ca2,2	Q2	Ca3,1	Ca3,2	Q3				
0.0037	0.3258	-9.71E+04	0.0002	0.1003	-3.06E+04				
0.9981	0.9053	2.81	0.9999	0.9709	0.89	kg/s			
		7.04E-04			2.22E-04	$/s			
4	CSTR	continued							
Ca2,1	Ca2,2	Q2	Ca3,1	Ca3,2	Q3	Ca4,1	Ca4,2	Q4	
0.0087	0.5857	-1.10E+05	0.0006	0.2417	-4.66E+04	0.0000	0.0997	-1.93E+04	
0.9954	0.8297	3.17	0.9997	0.9297	1.35	1.0000	0.9710	0.56	kg/s
		7.94E-04			3.37E-04			1.40E-04	$/s

Crystallizers and Recrystallizers

Crystallization		Cooling Agent		CaCl2 Brine							
T start (K)	T end (K)	Q (J/s)	Tin (K)	Tout (K)	U (W/m2K)	radius (m)	volume (m3)	time (h)	Cp (J/gK)	mass (kg)	Cost ($/s)
353	315	-6.29E+05	243	253	100.00	1.96	80.41	3.97	2.70	23.31	0.01
315	288	-3.76E+05	243	253	100.00	1.96	80.89	4.00	2.70	13.93	0.00

Recrystallization		Cooling Agent		CaCl2 Brine							
T start (K)	T end (K)	Q (J/s)	Tin (K)	Tout (K)	U (W/m2K)	radius (m)	volume (m3)	time (h)	Cp (J/gK)	mass (kg)	Cost ($/s)
353	315	-6.04E+05	243	253	100.00	1.92	75.56	3.73	2.70	22.37	0.01
315	288	-3.61E+05	243	253	100.00	1.92	76.01	3.76	2.70	13.36	0.00

Preheaters

Water+Recycle1					Heating Agent		5 atm Steam			
T in	T out	Flow rate	Heat capacity	Energy needed	Tin	Tout	U	Area	Mass	Cost
K	K	kg/min	J/gK	J/s	K	K	W/m2K	m2	kg/s	$/s
293	327	145.58	3.034	2.50E+05	425	425	310	7.047	0.1187	1.42E-03

Acetic Anhydride					Heating Agent		5 atm Steam			
T in	T out	Flow rate	Heat capacity	Energy needed	Tin	Tout	U	Area	Mass	Cost
298	326.7	138.69	1.648	1.09E+05	425	425	310	3.142	0.0518	6.22E-04

Recycle2					Heating Agent		5 atm Steam			
T in	T out	Flow rate	Heat capacity	Energy needed	Tin	Tout	U	Area	Mass	Cost
303.2	353	257.40	2.444	5.22E+05	425	425	310	17.783	0.2478	2.97E-03

Wash Heat Exchangers

Filter 1, 8:2 Wash				Cooling Agent		Chilled water				
T in	T out	Flow rate	Heat capacity	Energy needed	Tin	Tout	U	Area	Mass	Cost
K	K	kg/min	J/gK	J/s	K	K	W/m2K	m2	kg/s	$/s
349.8	288	33.05	2.48	-8.45E+04	278	283	100	33.70	4.04	1.62E-03
Filter 1, Water Wash				**Cooling Agent**		**Chilled water**				
T in	T out	Flow rate	Heat capacity	Energy needed	Tin	Tout	U	Area	Mass	Cost
298	288	33.05	4.21	-2.32E+04	278	283	100	21.45	1.11	4.44E-04
Filter 2, 8:2 Wash					**Cooling Agent**	**Chilled water**				
T in	T out	Flow rate	Heat capacity	Energy needed	Tin	Tout	U	Area	Mass	Cost
349.8	288	31.71	2.48	-8.11E+04	278	283	100	32.34	3.88	1.55E-03
Filter 2, Water Wash				**Cooling Agent**		**Chilled water**				
T in	T out	Flow rate	Heat capacity	Energy needed	Tin	Tout	U	Area	Mass	Cost
298	288	31.71	4.21	-2.23E+04	278	283	100	20.58	1.06	4.26E-04

A.6: Distillation

Batch

	mol fraction	mass fraction			
Acetic acid x	0.490	0.762			
Acetic acid y	0.341	0.633			
Water x	0.510	0.238			
Water y	0.659	0.367			
Tin	288	K			
Tout	380	K			
Initial	26.86	g API/kg solvent			
Final	200	g API/kg solvent			
		Total	Acetic Acid	Water	Acetaminophen
Distillate	kg/cycle	43,691	27,637	16,054	
Bottoms Solvent	kg/cycle	6,777	5,164	1,613	
Bottoms	kg/cycle	8,133	5,164	1,613	1,355
Distillate Recycle	kg/cycle	9,988	6,318	3,670	
Distillate Sell	kg/cycle	33,703	21,319	12,384	
Acetic Acid Buy	kg/cycle	8,362	8,362		
	Condensing			Heating	Boiling
Acetic Acid	-2.38E+07		Acetic Acid	6.19E+06	2.38E+07
Water	-3.62E+07		Water	6.85E+06	3.62E+07
Total (kJ/cycle)	-6.00E+07		Acetaminophen	1.57E+05	
			Total (kJ/cycle)	7.32E+07	
Cooling Agent: NaCl Brine			Heating Agent:5 atm steam		
Energy	-6.00E+07	kJ/cycle	Energy	7.32E+07	kJ/cycle
T in	263	K	T in	425	K
T out	273	K	T out	425	K
U	100	W/m2K	U	310	W/m2K
Time	60	min/cycle	Time	60	min/cycle
Area	1489	m2	Area	794	m2
Heat Capacity	3.45	J/gK	Condensation	2,107.40	J/g
Mass	1738876.16	kg	Mass	34,726.17	kg
Cost	434.7190399	$	Cost	416.71	$

Continuous

	mol fraction	mass fraction
Acetic acid x	0.490	0.762
Acetic acid y	0.347	0.639
Water x	0.510	0.238
Water y	0.653	0.361
T in	288	K
T out	380	K
Initial	27.49	g API/kg solvent
Final	200	g API/kg solvent

		Total	Acetic Acid	Water	Acetaminophen
Distillate	kg/min	309.99	198.06	111.93	
Bottoms Solvent	kg/min	49.40	37.64	11.76	
Bottoms	kg/min	59.28	37.64	11.76	9.88
Distillate Recycle	kg/min	70.40	44.98	25.42	
Distillate Sell	kg/min	239.58	153.08	86.51	
Acetic Acid Buy	kg/min	56.70	56.70		

ID	Condensing			Heating	Boiling
Acetic Acid	-1.70E+05		Acetic Acid	4.45E+04	1.70E+05
Water	-2.53E+05		Water	4.79E+04	2.53E+05
Total (kJ/min)	-4.23E+05		Acetaminophen	1.14E+03	
			Total (kJ/min)	5.16E+05	

Cooling Agent: NaCl Brine			Heating Agent: 5 atm steam		
Energy	-7.05E+06	J/s	Energy	8.61E+06	J/s
T in	263	K	T in	425	K
T out	273	K	T out	425	K
U	100	W/m2K	U	310	W/m2K
Area	630	m2	Area	336	m2
Heat Capacity	3.45	J/gK	Condensation	2107	J/g
Mass	204.29	kg/s	Mass	4.08	kg/s
Cost	0.0511	$/s	Cost	0.0490	$/s

A.7: Bare Module Costing

Table A.7: Batch Equipment Correlation Assumptions and Associated Cost

Unit Name		Unit Assumptions		Size	Units	Costing Size	Units	FBM	FM	Fd	Fp
Water Storage	V-101	cone roof, carbon steel		1,667,066.40	kg	441,717.42	gal	4	1	1	1
P-A storage	V-103	cone roof, carbon steel		1,415,039.32	kg	330,808.64	gal	4	1	1	1
AA storage	V-102	cone roof, polypropylene lined		3,706,513.51	kg	906,626.93	gal	4	1.9	1	1
Heated Storage H2O	V-105	hastelloy, P vessel		22,011.75	kg	5,832.38	gal	4.16	4.5	1	1
			eqtn 16.56	15.82	L(ft)	7.91	D(ft)				
			hastelloy, driver, agitator			8.75	hp	3.3	4.5	1	1
	HX-101		HE	7.92	m^2	85.2	ft^2	1.8	2	1	1
Heated Storage AA	V-106	hastelloy, P vessel,		22,062.58	kg	5,396.59	gal	4.16	4.5	1	1
			eqtn 16.56	15.42	L(ft)	7.71	D(ft)				
			hastelloy, driver, agitator			8.09	hp	3.3	4.5	1	1
	HX-102		HE	3.34	m^2	35.9	ft^2	1.8	2	1	1
Reactor 1	R-101	V pressure, hastelloy		19,935.16	kg						
				40.41	m^3	10,696.57	gal	4.16	4.5	1	1
			eqtn 16.56	19.36	L(ft)	9.68	D(ft)				
			hastelloy, driver, agitator			16.04	hp	3.3	4.5	1	1
		Jacket (P vessel + 6")		22,428.55	kg						
			hastelloy					4.16	4.5	1	1
		eqtn 16.54 16.56, 16.59 * 9/16", 0.297lb/in^3		20.86	L(ft)	10.18	D(ft)				
storage 21	V-107			19,935.16	kg						
		hastelloy, P vessel		40.41	m^3	10,696.57	gal	4.16	4.5	1	1
			eqtn 16.56	19.36	L(ft)	9.68	D(ft)				
			hastelloy, driver, agitator			16.04	hp	3.3	4.5	1	1
Agitated Nutsche Filter	NFD-101	filter, hastelloy, rotary-drum vac,		211.2	ft^2	211.2	ft^2	2.32	4.5	1	1
Water heat ex	HX-104			90.28	m^2	971.44	ft^2	1.8	2	1	1
8:2 heat ex	HX-105			134.98	m^2	1,452.36	ft^2	1.8	2	1	1

P4 heating dissolving	V-110			19,935.16	kg						
		V pressure, hastelloy		40.83	m^3	10,808.78	gal	4.16	4.5	1	1
			eqtn 16.56	19.43	L(ft)	9.72	D(ft)				
			hastelloy, driver, agitator			16.21	hp	3.3	4.5	1	1
		Jacket (P vessel + 6")		22,575.81	kg						
			hastelloy					4.16	4.5	1	1
		eqtn 16.54 16.56, 16.59 * 9/16", 0.297lb/in^3		20.93	L(ft)	10.22	D(ft)				
storage p15	V-111			20,074.00	kg						
		hastelloy, P vessel,		40.83	m^3	10,808.78		4.16	4.5	1	1
			eqtn 16.56	19.43	L(ft)	9.72	D(ft)				
			hastelloy, driver, agitator			16.21	hp	3.3	4.5	1	1
	HX-103		HE	27.64	m^2	297.39	ft^2	1.8	2	1	1
	GAC-101			18,600.75	kg						
Carbon Treatment		P vessel, hastelloy		1,288.54	ft^3	9,638.28	gal	4.16	4.5	1	1
1ft/min				18.7	L(ft)	9.35	D(ft)				
		10HP/1000gal				96.38	hp	3.3	4.5	1	1
Crystallizer	V-112	crystalliser (fbm),hastelloy, autoclave cO		48.04	m^3	12,716.21	gal	2.06	4.5	1	1
	V-113			22,365.47	kg						
storage p22		hastelloy, P vessel,		48.04	m^3	12,716.21	gal	4.16	4.5	1	1
			eqtn 16.56	20.51	L(ft)	10.26	D(ft)				
			hastelloy, driver, agitator			19.07	hp	3.3	4.5	1	1
ANF2	NFD-102	filter, hastelloy, rotary-drum vac,		188.68	ft^2	188.68	ft^2	2.32	4.5	1	1
	V-115			14,880.75	kg						
storage p13				26.03	m^3	6,890.60	gal	4.16	4.5	1	1
		hastelloy, P vessel,		16.72	L(ft)	8.36	D(ft)				
			eqtn 16.56			10.34	hp	3.3	4.5	1	1
			hastelloy, driver, agitator								
	V-109?			9,003.67	kg						
storage p17				12.22	m^3	3,235.26	gal	4.16	4.5	1	1
		hastelloy, P vessel,		13	L(ft)	6.5	D(ft)				

			eqtn 16.56			4.85	hp	3.3	4.5	1	1
			hastelloy, driver, agitator								
batch distillaiton	V-116	hastelloy, vertical pressure		35,878.68	kg						
				97.74	m^3	25,874.41	gal	4.16	4.5	1	1
				26	L(ft)	13	D(ft)				
Cooling ex				1,488.87	m^2	16,026.02	ft^2	1.8	2	1	1
Heating ex				793.54	m^2	8,541.63	ft^2	1.8	2	1	1
Bottoms Storage	V-117	cone roof, stainless steel		1,113.31	m^3	294,714.73	gal	4	2	1	1
Tops Storage	V-118	cone roof, stainless steel		5,557.76	m^3	1,471,250.31	gal	4	2	1	1
	V-119?			11,611.56							
Storage p-		hastelloy, P vessel,		17.92	m^3	4,744.32	gal	4.16	4.5	1	1
			eqtn 16.56	14.77	L(ft)	7.38	D(ft)				

Unit Name		Cpl	Cv	16.32 cost (Cp)	Cost	Cost Index	Quantity	Site Factor	Spares	Total Fab Eq	Total Spares	Total Storage
Water Storage	V-101			208,548	834,190	1,176,988	1	0.85	0		0	1,000,440
				179,800	719,199	1,014,742	1	0.85	0		0	862,531
P-A storage	V-103			301,583	1,477,756	2,085,018	1	0.85	0		0	1,772,265
								0.85				
AA storage	V-102	13,327	77,736	363,138	1,510,655	2,131,435	1	0.85	0		0	1,811,720
								0.85				0
Heated Storage H2O	V-105			14,132	96,101	135,592	1	0.85	0		0	115,253
				2,931	8,206	11,578	1	0.85	0			9,841
								0.85				
	HX-101	12,837	77,851	363,167	1,510,774	2,131,603	1	0.85	0		0	1,811,863
								0.85				
Heated Storage AA	V-106			13,521	91,939	129,721	1	0.85	0		0	110,263
				2,552	7,146	10,083	1	0.85	0		0	8,570
								0.85				
	HX-102	17,854	72,962	346,181	1,440,113	2,031,905	4	0.85	1	6,908,477	1,727,119	
Reactor 1	R-101				0	0	1	0.85	0	0	0	
				19,969	135,789	191,589	1	0.85	0	162,851	0	
								0.85				
		19,535	78,678	373,586	1,554,119	2,192,761	4	0.85	1	7,455,387	1,863,847	
					0	0	1	0.85	0	0	0	
								0.85				
		17,854		72,962	346,181	1,440,113	2,031,905	1	0.85	0	0	1,727,119
storage 21	V-107							0.85				
				19,969	135,789	191,589	1	0.85	0	0	0	162,851
								0.85				
				234,130	1,362,636	1,922,591	2	0.85	0	3,268,405	0	
				4,326	12,113	17,090	1	0.85	0	14,527	0	
Agitated Nutsche Filter	NFD-101			4,614	12,918	234,129.96	1,362,636.36	1,922,590.99	2.00	0.85	0.00	3,268,404.67
								0.85				
Water heat ex	HX-104			4,326.03	12,112.87	17,090.47	1.00	0.85	0.00	14,526.90	0.00	
8:2 heat ex	HX-105			4,613.54	12,917.92	18,226.34	1.00	0.85	0.00	15,492.39	0.00	
P4 heating dissolving	V-110	17,944.00	72,961.55	346,270.98	1,440,487.30	2,032,433.58	1.00	0.85	0.00	1,727,568.54	0.00	17,944.00
					0.00	0.00	1.00	0.85	0.00	0.00	0.00	
				20,088.06	136,598.79	192,731.97	1.00	0.85	0.00	163,822.18	0.00	
		19,627.41		79,009.85	375,171.73	1,560,714.41	2,202,066.18	1.00	0.85	1.00	1,871,756.25	1,871,756.25
						0.00	0.00	1.00	0.85	0.00	0.00	0.00

storage p15	V-111	17,944.00	73,285.10	347,726.97	1,446,544.21	2,040,979.48	1.00	0.85	0.00	0.00	0.00	1,734,832.56
								0.85				0.00
				20,088.06	136,598.79	192,731.97	1.00	0.85	0.00	0.00	0.00	163,822.18
				3,579.61	10,022.91	14,141.67	1.00	0.85	0.00		0.00	12,020.42
	HX-103	17,944.00	73,285.10	347,726.97	1,446,544.21	2,040,979.48	1.00	0.85	0.00	0.00	0.00	1,734,832.56
	GAC-101	16,979.29	69,817.46	331,157.85	1,377,616.67	1,943,727.22	1.00	0.85	0.00	1,652,168.14	0.00	
Carbon Treatment								0.85		0.00		
1ft/min				55,487.22	377,313.12	532,364.19	1.00	0.85	0.00	452,509.56	0.00	
								0.85				
Crystallizer	V-112	161,430.06	897,551.15	1,266,386.11	4.00	0.85	1.00	4,305,712.76	1,076,428.19	161,430.06	897,551.15	1,266,386.11
	V-113							0.85				0
storage p22		19,406.62	78,535.83	372,817.86	1,550,922.28	2,188,250.13	1.00	0.85	0.00		0.00	1,860,012.61
								0.85				0.00
				22,037.85	149,857.35	211,438.94	1.00	0.85	0.00		0.00	179,723.10
								0.85				
ANF2	NFD-102			223,899.22	1,303,093.47	1,838,579.86	6.00	0.85	1.00	9,376,757.26	1,562,792.88	
								0.85				
	V-115				0	0	1	0.85	0	0	0	
storage p13		14,443	60,674	287,477	1,195,905	1,687,343	1	0.85	0		0	1,434,242
								0.85				0
				15,541	105,682	149,110	1	0.85	0		0	126,744
					0	0	1	0.85	0	0	0	
								0.85				
	V-109?							0.85				
storage p17		10,031	44,604	210,751	876,722	1,236,998	1	0.85	0		0	1,051,448
								0.85				0
				10,100	68,682	96,906	1	0.85	0		0	82,370
					0	0	1	0.85	0		0	0
					0	0	1	0.85	0	0	0	
batch distillaiton	V-116							0.85				
		27,334	106,956	508,636	2,115,927	2,985,435	1	0.85	1	2,537,620	2,537,620	
					0	0	1	0.85	0	0	0	
Cooling ex				132,023	237,642	335,297	1	0.85	0	285,002	0	
								0.85				
Heating ex				73,784	132,812	187,388	1	0.85	0	159,280	0	
								0.85				
Bottoms Storage	V-117			169,452.90	847,264.52	1,195,434.95	1.00	0.85	0.00		0.00	1,016,119.71
								0.85				
Tops Storage	V-118			386,606	1,933,032	2,727,382	1	0.85	0		0	2,318,275

Storage p-	12,064	52,047	246,278	1,024,516	1,445,525	1	0.85	0		0	1,228,696
Total			5,601,951	24,983,866	35,250,604	59	0.85	5	40,357,335	10,639,563	20,601,021

Table A.9: Continuous Equipment Correlation Assumptions and Associated Cost

Unit Name		Unit Assumptions		**Size**	**Units**	**Costing Size**	**Units**	**FBM**	**FM**	**Fd**	**Fp**
Water Storage	V-101	cone roof, carbon steel		1,243,999.37	kg	329,618.66	gal	1	1	1	1
P-A storage	V-103	cone roof, carbon steel		1,067,422.92	kg	249,542.70	gal	1	1	1	1
AA storage	V-102	cone roof, polypropylene lined		2,795,977.07	kg	683,906.35	gal	1	1.9	1	1
Heat exchanger H2O	HX-101			7.05	m^2	75.82	ft^2	1.8	2	1	1
Heat exchanger AA	HX-102			3.14	m^2	33.81	ft^2	1.8	2	1	1
Reactor 1 (CSTR)	R-101			7,415.43	kg						
				9.12	m^3	2,415.50	gal	4.16	4.5	1	1
			eqtn 16.56	11.79	L(ft)	5.9	D(ft)				
			hastelloy, driver, agitator			3.62	hp	3.3	4.5	1	1
		Jacket (P vessel + 6")		8,964.51	kg						
			hastelloy					4.16	4.5	1	1
			eqtn 16.54 16.56, 16.59 * 9/16", 0.297lb/in^3	13.29	L(ft)	6.4	D(ft)				
Reactor 2 (CSTR)	R-102			8,260.56	kg						
				10.73	m^3	2,841.76	gal	4.16	4.5	1	1
			eqtn 16.56	12.45	L(ft)	6.22	D(ft)				
			hastelloy, driver, agitator			4.26	hp	3.3	4.5	1	1
		Jacket (P vessel + 6")		9,891.50	kg						
			hastelloy					4.16	4.5	1	1
			eqtn 16.54 16.56, 16.59 * 9/16", 0.297lb/in^3	13.95	L(ft)	6.72	D(ft)				
Reactor 3 (MSMPR)	V-105			35,106.87	kg						
				94.6	m^3	25,042.54	gal	4.16	4.5	1	1
			eqtn 16.56	25.71	L(ft)	12.86	D(ft)				
			hastelloy, driver, agitator			37.56	hp	3.3	4.5	1	1
		Jacket (P vessel + 6")		38,391.94	kg						
			hastelloy					4.16	4.5	1	1
			eqtn 16.54 16.56, 16.59 * 9/16", 0.297lb/in^3	27.21	L(ft)	13.36	D(ft)				
Reactor 4 (MSMPR)	V-106			35,246.84	kg						
				95.17	m^3	25,192.73	gal	4.16	4.5	1	1

			eqtn 16.56	25.76	L(ft)	12.88	D(ft)				
			hastelloy, driver, agitator			37.79	hp	3.3	4.5	1	1
	W	Jacket (P vessel + 6")		38,538.30	kg						
			hastelloy					4.16	4.5	1	1
			eqtn 16.54 16.56, 16.59 * 9/16", 0.297lb/in^3	27.26	L(ft)	13.38	D(ft)				
				1,712.80	kg						
Reactor 5 (MSMPR)				1	m^3	264.72	gal	4.16	4.5	1	1
				eqtn 16.56	5.64	L(ft)	2.82	D(ft)			
			hastelloy, driver, agitator			0.4	hp	3.3	4.5	1	1
	W	Jacket (P vessel + 6")		2,495.06	kg						
			hastelloy					4.16	4.5	1	1
			eqtn 16.54 16.56, 16.59 * 9/16", 0.297lb/in^3	7.14	L(ft)	3.32	D(ft)				
Screw Press	14000lb/hr		SP-101	3,965.94	kg/hr	8,740.94	lb/hr	2.32	4.5	1	1
Water heat ex	HX-104			33.71	m^2	362.69	ft^2	1.8	2	1	1
8:2 heat ex	HX-105			21.45	m^2	230.78	ft^2	1.8	2	1	1
Solvent heat ex	HX-103			17.78	m^2	191.34	ft^2	1.8	2	1	1
CSTR dissolving	30 minutes		V-107	7.43	m^3	1,966.37	gal	4.16	4.5	1	1
Carbon Treatment	GAC-101			371.02	ft^3	2,775.26	gal	4.16	4.5	1	1
				12.35	L(ft)	6.18	D(ft)				
	V-108			33,682.61	kg						
Reactor 6 (MSMPR)				88.89	m^3	23,531.48	gal	4.16	4.5	1	1
			eqtn 16.56	25.19	L(ft)	12.59	D(ft)				
			hastelloy, driver, agitator			35.3	hp	3.3	4.5	1	1
	W	Jacket (P vessel + 6")		36,901.85	kg						
			hastelloy					4.16	4.5	1	1
			eqtn 16.54 16.56, 16.59 * 9/16", 0.297lb/in^3	26.69	L(ft)	13.09	D(ft)				
	V-109			33,816.20	kg						
Reactor 7 (MSMPR)				89.42	m^3	23,671.88	gal	4.16	4.5	1	1
			eqtn 16.56	25.24	L(ft)	12.62	D(ft)				

			hastelloy, driver, agitator			35.51	hp	3.3	4.5	1	1
	W	Jacket (P vessel + 6")		37,041.6 7	kg						
			hastelloy					4.16	4.5	1	1
			eqtn 16.54 16.56, 16.59 * 9/16", 0.297lb/in^3	26.74	L(ft)	13.12	D(ft)				
Reactor 8 (MSMPR)				1,712.80	kg						
				1	m^3	264.72	gal	4.16	4.5	1	1
			eqtn 16.56	5.64	L(ft)	2.82	D(ft)				
			hastelloy, driver, agitator			0.4	hp	3.3	4.5	1	1
	W	Jacket (P vessel + 6")		2,495.06	kg						
			hastelloy					4.16	4.5	1	1
			eqtn 16.54 16.56, 16.59 * 9/16", 0.297lb/in^3	7.14	L(ft)	3.32	D(ft)				
Screw Press	SC-102			3,805.18	kg/hr	8,386.61	lb/hr	2.32	4.5	1	1
Water heat ex	HX-106			32.34	m^2	347.99	ft^2	1.8	2	1	1
8:2 heat ex	HX-107			20.58	m^2	221.42	ft^2	1.8	2	1	1
Fluid Bed Drying	0.5	indirect heat rotary		698.88	ft^3	1,397.77	ft^2	2.06	2	1	1
	FBDR-101				6:1 L:D						
				63.41958 397	kg/min						
distillaiton	C-101	hastelloy, vertical pressure		6,390.04	kg						
260.44416	ft^3			7.29	m^3	1,930.45	gal	4.16	4.5	1	1
Cooling ex				629.71	m^2	6,778.14	ft^2	1.8	2	1	1
Heating ex				335.99	m^2	3,616.53	ft^2	1.8	2	1	1
Bottoms Storage	V-111	cone roof, stainless steel		973.79	m^3	257,782.31	gal	4	2	1	1
Tops Storage	V-112	cone roof, stainless steel		4,740.15	m^3	1,254,811.97	gal	4	2	1	1

Unit Name	Unit Assumptions	Cpl	Cv	**16.32 cost (Cp)**	**Cost**	**Cost Index**	**Quantity**	**Site Factor**	**Spares**	**Total**	**Total Spares**	**Total Storage**
Water Storage	V-101			179,468	179,468	253,217	1	0.85	0		0	215,234.44
P-A storage	V-103			155,590	155,590	219,527	1	0.85	0		0	186,598.03
AA storage	V-102			260,975	495,853	699,616	1	0.85	0		0	594,673.52
								0.85				
Heat exchanger H2O	HX-101			2,877	8,054	11,364	1	0.85	0	9,660	0	
Heat exchanger AA	HX-102			2,528	7,078	9,987	1	0.85	0	8,489	0	
	R-101	8,713	39,729	187,495	779,978	1,100,498	1	0.85	1	935,424	935,424	
Reactor 1 (CSTR)					0	0	1	0.85	0	0	0	
				8,551	58,144	82,038	1	0.85	0	69,732	0	
	W	10,071	44,488	210,265	874,704	1,234,150	1	0.85	1	1,049,027	1,049,027	
					0	0	1	0.85	0	0	0	
								0.85				
								0.85		0	0	
Reactor 2 (CSTR)	R-102	9,423	42,362	200,051	832,211	1,174,195	1	0.85	0	998,066	0	
				9,381	63,788	90,001	1	0.85	0	76,501	0	
								0.85				
	W	10,812	47,207	223,244	928,694	1,310,327	1	0.85	1	1,113,778	1,113,778	
					0	0	1	0.85	0	0	0	
								0.85				
									0.85		0	
Reactor 3 (MSMPR)	V-105	26,906	105,423	501,311	2,085,452	2,942,437	1	0.85	1	2,501,071	2,501,071	
				32,429	220,516	311,134	1	0.85	0	264,464	0	
								0.85				
	W	28,808	111,889	532,307	2,214,398	3,124,371	1	0.85	1	2,655,716	2,655,716	
					0	0	1	0.85	0	0	0	
Reactor 4 (MSMPR)	V-106	26,984	105,702	502,642	2,090,992	2,950,254	1	0.85	0	2,507,716	0	
					0	0	1	0.85	0	0	0	
				32,540	221,269	312,196	1	0.85	0	265,367	0	
								0.85				
	W	28,887	112,173	533,667	2,220,056	3,132,354	1	0.85	1	2,662,501	2,662,501	
Screw Press	14000lb/hr			318,402	1,853,098	2,614,600	1	0.85	1	2,222,410	2,222,410	
Water heat ex	HX-104			3,695	10,346	14,598	1	0.85	0	12,408	0	
8:2 heat ex				3,437	9,624	13,579	1	0.85	0	11,542	0	

Solvent heat ex	HX-105			3,336	9,340	13,178	1	0.85	0	11,202	0	
CSTR dissolving	HX-103			61,154	468,439	660,937	1	0.85	0	561,796	0	
Carbon Treatment	GAC-101			9,316	71,360	100,684	1	0.85	0	85,581	0	
								0.85				
Reactor 6 (MSMPR)	V-108	26,111	102,570	487,677	2,028,738	2,862,417	1	0.85	1	2,433,054	2,433,054	
				31,299	212,831	300,290	1	0.85	0	255,247	0	
								0.85				
	W	27,996	108,975	518,383	2,156,473	3,042,642	1	0.85	1	2,586,246	2,586,246	
	V-109	26,186	102,839	488,963	2,034,085	2,869,961	1	0.85	0	2,439,466	0	
Reactor 7 (MSMPR)					0	0	1	0.85	0	0	0	
				31,405	213,554	301,310	1	0.85	0	256,114	0	
								0.85				
	W	28,072	109,250	519,696	2,161,934	3,050,348	1	0.85	1	2,592,796	2,592,796	
					0	0	1	0.85	0	0	0	
Screw Press	SC-102			191,000	1,111,620	1,568,423	1	0.85	1	1,333,160	1,333,160	
Water heat ex	HX-106			3,671	10,278	14,502	1	0.85	0	12,326	0	
8:2 heat ex	HX-107			3,415	9,561	13,490	1	0.85	0	11,466	0	
Fluid Bed Drying	FBDR-101			499,105	1,527,260	2,154,864	1	0.85	1	1,831,635	1,831,635	
								0.85				
distillaiton	C-101	7,820	36,398	171,610	713,897	1,007,262	1	0.85	1	856,173	856,173	
260.44416	ft^3				0	0	1	0.85	0	0	0	
Cooling ex				60,761	109,370	154,314	1	0.85	0	131,167	0	
Heating ex				37,813	68,063	96,033	1	0.85	0	81,628	0	
Bottoms Storage	V-111			158,204	791,022	1,116,081	1	0.85	0		0	948,668.71
								0.85				
Tops Storage	V-112			356,301	1,781,504	2,513,585	1	0.85	0		0	2,136,547.64
Total									32,842,927.32	25,774,925.50	4,081,722.34	32,842,927.32

Pumps

Pump	kg/cycle	min/cycle	density	Q	H (ft)	S	CB ($)	FT	FM
PM-101	6657.8500	90.0000	1000.0000	50.0000	100.0000	500.0000	4360.2181	1.0000	1.0000
PM-107	4709.5580	30.0000	1000.0000	50.0000	100.0000	500.0000	4360.2181	1.0000	1.0000
PM-115	4756.4688	30.0000	1000.0000	50.0000	100.0000	500.0000	4360.2181	1.0000	1.0000
PM-103	18753.190	10.0000	1080.0000	458.7101	100.0000	4587.1006	5659.2126	1.0000	4.5000
PM-102	19708.662	10.0000	1043.9310	498.7376	100.0000	4987.3763	5810.7807	1.0000	4.5000
PM-104	18753.190	10.0000	1080.0000	458.7101	100.0000	4587.1006	5659.2126	1.0000	4.5000
PM-105	46096.930	15.0000	1342.1322	604.8841	100.0000	6048.8414	6204.4958	1.0000	4.5000
PM-106	46096.930	80.0000	1342.1322	113.4158	100.0000	1134.1578	4350.2283	1.0000	4.5000
PM-108	36677.810	240.0000	1067.8632	50.0000	100.0000	500.0000	4360.2181	1.0000	4.5000
	4709.5580	30.0000	1023.8569	50.0000	100.0000	500.0000	4360.2181	1.0000	4.5000
	4709.5580	30.0000	1000.0000	50.0000	100.0000	500.0000	4360.2181	1.0000	4.5000
PM-125	8883.5831	10.0000	1023.8569	229.2111	100.0000	2292.1114	4761.6923	1.0000	4.5000
PM-124	4709.5580	30.0000	1023.8569	50.0000	100.0000	500.0000	4360.2181	1.0000	4.5000
PM-126	4756.4688	30.0000	1023.8569	50.0000	100.0000	500.0000	4360.2181	1.0000	4.5000
PM-110	36679.808	15.0000	1056.8616	611.2297	100.0000	6112.2969	6227.6735	1.0000	4.5000
PM-111	46098.924	60.0000	1328.2563	152.8074	100.0000	1528.0742	4473.1902	1.0000	4.5000
PM-112	46098.924	60.0000	1328.2563	152.8074	100.0000	1528.0742	4473.1902	1.0000	4.5000
PM-113	46574.571	15.0000	1341.9612	611.2297	100.0000	6112.2969	6227.6735	1.0000	4.5000
PM-114	46574.571	120.0000	1341.9612	76.4037	100.0000	764.0371	4292.6167	1.0000	4.5000
PM-116	37061.633	240.0000	1067.8632	50.0000	100.0000	500.0000	4360.2181	1.0000	4.5000
	4756.4688	30.0000	1023.8569	50.0000	100.0000	500.0000	4360.2181	1.0000	4.5000
	4756.4688	30.0000	1000.0000	50.0000	100.0000	500.0000	4360.2181	1.0000	4.5000
PM-109	13050.820	10.0000	1067.8632	322.8560	100.0000	3228.5599	5132.0062	1.0000	4.5000
PM-127	23626.990	10.0000	1067.8632	584.4934	100.0000	5844.9343	6129.7519	1.0000	4.5000
PM-117	27796.225	10.0000	1067.8632	687.6334	100.0000	6876.3340	6503.8074	1.0000	4.5000
PM-128	9265.4084	10.0000	1067.8632	229.2111	100.0000	2292.1114	4761.6923	1.0000	4.5000
PM-118	18932.053	10.0000	1011.7878	494.3051	100.0000	4943.0507	5794.0826	1.0000	4.5000
PM-120	43691.000	20.0000	1018.7701	566.4621	100.0000	5664.6207	6063.3134	1.0000	4.5000
PM-122	9987.9667	10.0000	1018.7701	258.9928	100.0000	2589.9280	4879.2379	1.0000	4.5000
PM-123	8361.6432	10.0000	1030.0000	214.4575	100.0000	2144.5748	4703.9547	1.0000	4.5000
PM-119	8132.6960	10.0000	1227.2378	175.0623	100.0000	1750.6228	4553.5249	1.0000	4.5000
All									

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Pump	Pump CP	rho	np	PB (hp)	nm	PC (hp)	CB ($)	FT	Motor CP
PM-101	4360.2181	8.3454	0.4400	2.8739	0.8316	3.4557	443.0743	1.0000	443.0743
PM-107	4360.2181	8.3454	0.4400	2.8739	0.8316	3.4557	443.0743	1.0000	443.0743
PM-115	4360.2181	8.3454	0.4400	2.8739	0.8316	3.4557	443.0743	1.0000	443.0743
PM-103	25466.456	9.0130	0.7054	17.7601	0.8767	20.2576	958.5497	1.0000	958.5497
PM-102	26148.513	8.7120	0.7131	18.4631	0.8775	21.0396	986.4498	1.0000	986.4498
PM-104	25466.456	9.0130	0.7054	17.7601	0.8767	20.2576	958.5497	1.0000	958.5497
PM-105	27920.231	11.2006	0.7303	28.1130	0.8862	31.7243	1392.8612	1.0000	1392.8612
PM-106	19576.027	11.2006	0.5518	6.9763	0.8551	8.1585	565.7613	1.0000	565.7613
PM-108	19620.981	8.9117	0.4400	3.0689	0.8335	3.6821	448.2329	1.0000	448.2329
	19620.981	8.5445	0.4400	2.9425	0.8323	3.5353	444.8782	1.0000	444.8782
	19620.981	8.3454	0.4400	2.8739	0.8316	3.4557	443.0743	1.0000	443.0743
PM-125	21427.615	8.5445	0.6350	9.3462	0.8622	10.8399	645.5242	1.0000	645.5242
PM-124	19620.981	8.5445	0.4400	2.9425	0.8323	3.5353	444.8782	1.0000	444.8782
PM-126	19620.981	8.5445	0.4400	2.9425	0.8323	3.5353	444.8782	1.0000	444.8782
PM-110	28024.530	8.8199	0.7312	22.3422	0.8815	25.3448	1144.7108	1.0000	1144.7108
PM-111	20129.355	11.0848	0.5885	8.7220	0.8606	10.1353	624.0712	1.0000	624.0712
PM-112	20129.355	11.0848	0.5885	8.7220	0.8606	10.1353	624.0712	1.0000	624.0712
PM-113	28024.530	11.1992	0.7312	28.3693	0.8863	32.0070	1404.2158	1.0000	1404.2158
PM-114	19316.775	11.1992	0.4999	5.1872	0.8476	6.1199	509.1520	1.0000	509.1520
PM-116	19620.981	8.9117	0.4400	3.0689	0.8335	3.6821	448.2329	1.0000	448.2329
	19620.981	8.5445	0.4400	2.9425	0.8323	3.5353	444.8782	1.0000	444.8782
	19620.981	8.3454	0.4400	2.8739	0.8316	3.4557	443.0743	1.0000	443.0743
PM-109	23094.027	8.9117	0.6712	12.9896	0.8698	14.9335	776.0273	1.0000	776.0273
PM-127	27583.883	8.9117	0.7273	21.7026	0.8809	24.6360	1118.1270	1.0000	1118.1270
PM-117	29267.133	8.9117	0.7412	25.0541	0.8839	28.3459	1259.4927	1.0000	1259.4927
PM-128	21427.615	8.9117	0.6350	9.7479	0.8632	11.2927	659.4819	1.0000	659.4819
PM-118	26073.371	8.4438	0.7123	17.7558	0.8767	20.2529	958.3826	1.0000	958.3826
PM-120	27284.910	8.5020	0.7246	20.1423	0.8794	22.9052	1054.0779	1.0000	1054.0779
PM-122	21956.570	8.5020	0.6482	10.2935	0.8645	11.9071	678.6213	1.0000	678.6213
PM-123	21167.796	8.5958	0.6276	8.9002	0.8610	10.3366	630.1674	1.0000	630.1674
PM-119	20490.861	10.2418	0.6045	8.9874	0.8613	10.4351	633.1590	1.0000	633.1590
All									

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Pump	CP	CBM ($)	Number	Total	Efficiency	kW	kWhr/year	$/kWhr	$/year
PM-101	6777.1320	22365.000	1.0000	22365.000	0.9500	2.7125	14257.012	0.0700	997.9909
PM-107	6151.9831	20302.000	1.0000	20302.000	0.9500	2.7125	4752.3376	0.0700	332.6636
PM-115	6151.9831	20302.000	1.0000	20302.000	0.9500	2.7125	4752.3376	0.0700	332.6636
PM-103	35931.508	118574.00	1.0000	118574.00	0.9500	15.9011	9286.2700	0.0700	650.0389
PM-102	36893.845	121750.00	1.0000	121750.00	0.9500	16.5150	9644.7338	0.0700	675.1314
PM-104	35931.508	118574.00	1.0000	118574.00	0.9500	15.9011	9286.2700	0.0700	650.0389
PM-105	39393.624	129999.00	4.0000	519996.00	0.9500	24.9019	87256.177	0.0700	6107.9324
PM-106	27620.497	91148.000	5.0000	455738.00	0.9500	6.4040	149597.04	0.0700	10471.793
PM-108	27683.924	91357.000	5.0000	456785.00	0.9500	2.8902	202547.10	0.0700	14178.297
	27683.924	91357.000							
	27683.924	91357.000							
PM-125	30232.966	99769.000	1.0000	99769.000	0.9500	8.5087	4969.0921	0.0700	347.8364
PM-124	27683.924	91357.000	1.0000	91357.000	0.9500	2.7750	4861.8522	0.0700	340.3297
PM-126	27683.924	91357.000	1.0000	91357.000	0.9500	2.7750	4861.8522	0.0700	340.3297
PM-110	39540.784	130485.00	1.0000	130485.00	0.9500	19.8943	17427.405	0.0700	1219.9184
PM-111	28401.207	93724.000	1.0000	93724.000	0.9500	7.9557	27876.688	0.0700	1951.3682
PM-112	28401.207	93724.000	1.0000	93724.000	0.9500	7.9557	27876.688	0.0700	1951.3682
PM-113	39540.784	130485.00	3.0000	391454.00	0.9500	25.1238	66025.314	0.0700	4621.7720
PM-114	27254.709	89941.000	5.0000	449703.00	0.9500	4.8038	168326.38	0.0700	11782.846
PM-116	27683.924	91357.000	5.0000	456785.00	0.9500	2.8902	202547.10	0.0700	14178.297
	27683.924	91357.000							
	27683.924	91357.000							
PM-109	32584.166	107528.00	1.0000	107528.00	0.9500	11.7220	6845.6397	0.0700	479.1948
PM-127	38919.059	128433.00							
PM-117	41294.015	136270.00	1.0000	136270.00	0.9500	22.2500	12994.027	0.0700	909.5819
PM-128	30232.966	99769.000							
PM-118	36787.825	121400.00	1.0000	121400.00	0.9500	15.8975	9284.1139	0.0700	649.8880
PM-120	38497.227	127041.00	1.0000	127041.00	0.9500	17.9793	20999.878	0.0700	1469.9915
PM-122	30979.288	102232.00	1.0000	102232.00	0.9500	9.3465	5458.3342	0.0700	382.0834
PM-123	29866.379	98559.000	1.0000	98559.000	0.9500	8.1137	4738.3979	0.0700	331.6879
PM-119	28911.269	95407.000	1.0000	95407.000	0.9500	8.1910	4783.5361	0.0700	334.8475
All			46.0000	4541177.0					75687.891

A.8: Optimization Batch Time Length

Time (min)	Equipment cost	Operating cost	Comparison
90	$72,845,000	$9,798,000	$92,441,000
120	$70,560,000	$9,895,000	$90,350,000
150	$72,194,000	$9,968,000	$92,130,000

Section 24: Problem Statement

Production of Acetaminophen (Paracetamol / APAP) by Batch and Continuous Processes

Recommended by: Alex Marchut, Esperion and Art Etchells, Consultant

Background

Acetaminophen is an API (active pharmaceutical ingredient) in Tylenol® and other over the counter pain relief drugs. The current production rate globally is 80,000 metric tons per year. It is a typical small molecule chemical produced by a non-biological / synthetic process. The current global market value is $350 million dollars. A typical price in the US is $8 per kilogram but the project should include a sensitivity study to determine if it could be sold at a lower cost. The current batch process consists of starting with phenol, a commodity chemical, then turning that into nitro-phenol. There are two isomers which must be separated by distillation. Then the para isomer is converted into amino-phenol by hydrogenation. All are liquid phase reactions. The nitration requires two liquid phases and the hydrogenation is a gas liquid reaction with a solid catalyst. The last step is to add acetic anhydride which precipitates the final product. This crystal product is then recrystallized for purity and then converted into tablets with the addition of excipient which enhance digestibility. The solids handling steps to produce the tablets are outside of the scope of this project – it ends with the purified and dried acetaminophen crystals.

Project Statement

The product is an article of commerce and it has been suggested that one way to enhance profits is to reduce production costs by changing the process to a continuous process. The plant design is to be 30,000 metric tons / year batch or continuous, this large production rate may make continuous attractive.

Batch and continuous designs should be completed to do a thorough comparison, i.e., two manufacturing process trains will need to be designed: one batch and one continuous. There are several synthetic possibilities to make this API but it is recommended to focus on starting with p-nitro phenol, undergoing a hydrogenation, to p-amino phenol and then adding acetic anhydride to yield the API. Please consider the regulatory constraints mentioned in the appendix when defining which steps will be run under Good Manufacturing Practices (GMP). It might be more economic to buy the nitro-phenol rather than making it unless the continuous hydrogenation process is very economic under GMP constraints.

The solvent for the early steps is often given as benzene. This is an unpopular solvent because of health reasons. Other solvents should be considered such as toluene. For the crystallization, combinations of alcohols and water seem to work as solvents at elevated temperatures.

The current prime manufacturer is Mallinckrodt with a large plant in Raleigh NC Research Triangle Park. They have an extensive patent position as do several other companies.

As you design the facility, you should do your best to keep capital costs of the equipment and operating costs of the facility to a minimum. You can build the plant anywhere in the world, but you should consider things like cost of labor and availability of dependable supplies and utilities such as electricity and water when you choose the location. The facility should be designed so that the operators are safe from hazards like inhaling dust from the powders & solvents, no waste is released to the environment, and any risks of dust and / or solvent explosions are accounted for in the design (also note the flammability hazards related with hydrogen). The final design should compare a batch and a continuous process, ultimately making a recommendation as to which is a wiser investment.

Appendix: Some Regulatory Constraints

In the pharmaceutical industry, for regulatory purposes production is governed by US Food and Drug Administration Good Manufacturing Practices. The starting materials must be defined, and they must be commercially available (there must be at least 3 suppliers that make them). Whatever is done to make those raw materials (known as Regulatory Starting Materials or RSM's) is not subject to Good Manufacturing Practice. GMP facilities are extremely well regulated and subject to a variety of audits and therefore generally more expensive (for this work assume that materials made under GMP have a 50 percent increased cost added).

References

1. "Manufacturing & Effluent Treatment Process" Adroit Pharmaceuticals Pvt.Ltd. Amadi (V), Nagpur (D).
2. "Continuous Crystallization of Paracetamol (Acetaminophen) Form II: Selective Access to a Metastable Solid Form" L. R. Agnew et al., Cryst. Growth Des. 2017, 17, 5, 2418–2427

There is a video on YouTube of the final precipitation crystallization step