

**The Siting, Process Analysis and Design of a
Manufacturing Facility
Using Hazardous Materials in a
Residential Community
(The Manufacture of Aspirin)**

**Fundamentals of Engineering Design
Workbook**

By

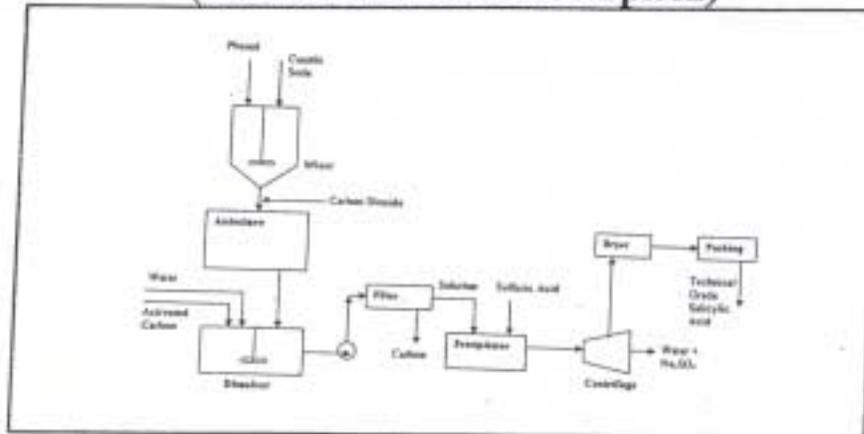
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I. Preface

1.1 Introduction

Of all medicines, aspirin, that little white pill, has probably been the most widely used and probably one of the most effective. As an analgesic agent, it has long been used to ease the pain of arthritis, ease headaches, reduce fever, and more recently, it has been shown to thin blood and prevents heart attacks and strokes. However, it is a medicine, and all medicines should be used with precaution under the advisement of a physician. It is known to irritate the stomach and can cause kidney damage and death. It is also a chemical, and all chemicals, including water, are toxic if not used in proper quantities. Aspirin, although taken internally by humans in small quantities, is manufactured by using many hazardous, toxic raw materials.

1.2 The Project Background

The Siting and the Process Analysis and Design of a Manufacturing Facility Using Hazardous Materials in a Residential Community (The Manufacture of Aspirin) is a joint cooperative project by Faculty from the Departments of Chemical Engineering, Chemistry and Environmental Science, and Civil and Environmental Engineering to introduce freshmen to design concepts and problems. The Chemical Engineers focus on the process analysis and design concepts while the Civil Engineers focus on Facility siting and related problems including:

- Visits to Potential Sites
- Environmental Restrictions
- Political Restrictions
- Economic Aspects Related to the Site
- Final Site Selection and Plant Layout

The Chemical Engineers are concerned with:

- The Process Concept
- Hazardous Materials and Health Considerations
 - Input – Output Flow Rates

- Material Balances Around the Process and the Process Units
- Estimating the Size of the Manufacturing Plant
- Raw Material Requirements
- Pollution Abatement and Prevention

Material balances concepts are introduced in the sophomore year in chemical engineering. It is, therefore, very understandable that these new concepts are not easily comprehended especially for freshmen who have never been exposed to this approach to problem solution. However, experiences have shown that with sufficient guidance, the freshmen can solve the presented problem and have an understanding of the problem and its solution, and thus, have a very meaningful, design-based experience.

This workbook follows the concept of a Freshman Chemistry Laboratory Workbook and is developed to guide the inexperienced students, step by step, through the process analysis of an aspirin manufacturing process. It is suggested that the students work through the workbook, as teams, and cooperate with each other for a meaningful learning experience. When difficulties are encountered, they should consult with their instructor to clarify the problem before proceeding.

In making the calculations and drawings, the student should apply the latest available computer technology such as EXCEL for the tabulation of the data and calculations and use graphic programs for flow sheets. The report should be written with a word processor such as WORD. In this manner, at the conclusion of the course, the student has progressed very well for a one-semester course in Freshman Engineering.

2. Background and History

2.1 Prepare a short history based on the literature for aspirin (6-8 pages, double spaced)

Your short history presentation should include:

- The beginning of the cure of headaches using willow bark (Chinese, 500 BC, Hippocrates, 400 BC)
- The isolation of the active ingredient in willow bark close to 200 years ago
- The beginning of synthetic production about 150-160 years ago
- The introduction from Europe to America about 100 years ago
- The present day aspects of aspirin production

Starting Reference:

Mann, Charles C. and Plummer, Mark L., "The Aspirin Wars," Harvard School Press, 1991

3. Hazardous Materials and Health

3.1 From the Materials Safety Data Sheets (MSDS) discuss the health hazards for each chemical used in this process.

For example, for the chemical phenol, discuss

- Inhalation
- Skin Contact
- Eye Contact
- Ingestion
- Target Organs
- Acute Effects
- Chronic Effects

Hint: Material Safety Data Sheets can be accessed through the Internet as outlined in the Appendix, Section 11.1. First access all of the Chemical Abstract Service Numbers (CAS Numbers) from

www.chemfinder.com

and then access the MSDS from

www.ilpi.com/msds/index.html#internet

4. Process Analysis and Design of a Hazardous Substance Manufacturing Facility

4.1 The Flow Sheet

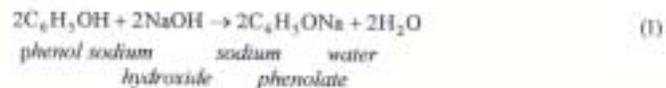
An extensive flow diagram for the manufacture of aspirin is available for review and analysis (7,8). For simplification in this study, a simplified flow sheet will be used. This study is based on the Schmitt modification of the Kolbe synthesis to manufacture aspirin (acetyl salicylic acid) from phenol in a two step process will be used.

4.2 The Chemistry of the Process (Kolbe-Schmitt Synthesis)

The chemical reaction to produce Aspirin (acetyl salicylic acid) is a result of a two step process involving numerous reactions of materials. The processes are shown in Figures 1 and 2 and each step is explained by the following explanation.

Step 1

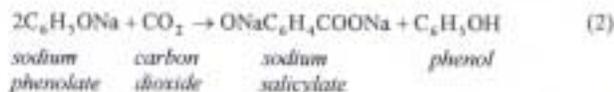
1. **MIXER:** The manufacturing of Aspirin begins when phenol is mixed with caustic soda (sodium hydroxide) with sodium phenolate the product that is produced in this process. The chemical reaction of interest is:



2. **AUTOCLAVE:** The sodium phenolate that is produced is dried in an autoclave to a finely divided powder. The autoclave is a revolving, heated ball mill. It operates under vacuum and at a temperature of 130°C. Water is removed from the process.

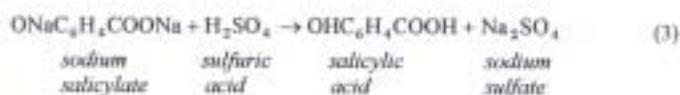
When drying of the sodium phenolate is complete, carbon dioxide gas is introduced under a pressure of 700 kPa and a temperature of 100°C. Sodium phenol

carbonate is formed and this in turn reacts to sodium salicylate. Phenol is regenerated and recovered for recycle. The governing chemical reaction equation is:



3. **DISSOLVER:** Water dissolves the sodium salicylate and activated carbon is added to remove color by adsorption. The solid activated carbon is removed in a filter, reactivated and recycled.

4. **PRECIPATOR:** The sodium salicylate solution is mixed with sulfuric acid, which precipitates the salicylic acid. The chemical reaction equation is:

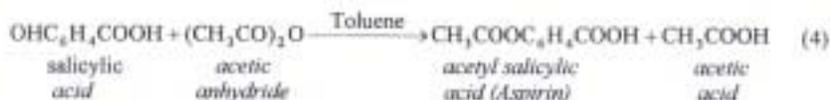


5. **CENTRIFUGE:** The precipitate, salicylic acid, is removed from sodium sulfate solution and sent to another drier.

6. **DRIER:** The salicylic acid is purified by sublimation, sent to packing and finally sold.

Step II

1. **REACTOR:** The salicylic acid is mixed with toluene and acetic anhydride and refluxed in a reactor at 88 - 92°C for approximately twenty hours. The chemical reaction equation is:



The reactor effluent passes through cooling tanks and, hence, to a filter. The filtrate is recovered and recycled, and the filter solid, which contains the product acetyl salicylic acid is sent to a washer. The washed product is dried and packaged for sale as Aspirin.

4.3 The Simplified Process of Manufacturing Aspirin

The flow diagram for Step I of the process is shown in Figure 1 and Step II is shown in Figure 2. To better understand the processes, you may wish to write the chemical reaction equations and process action on the diagram.

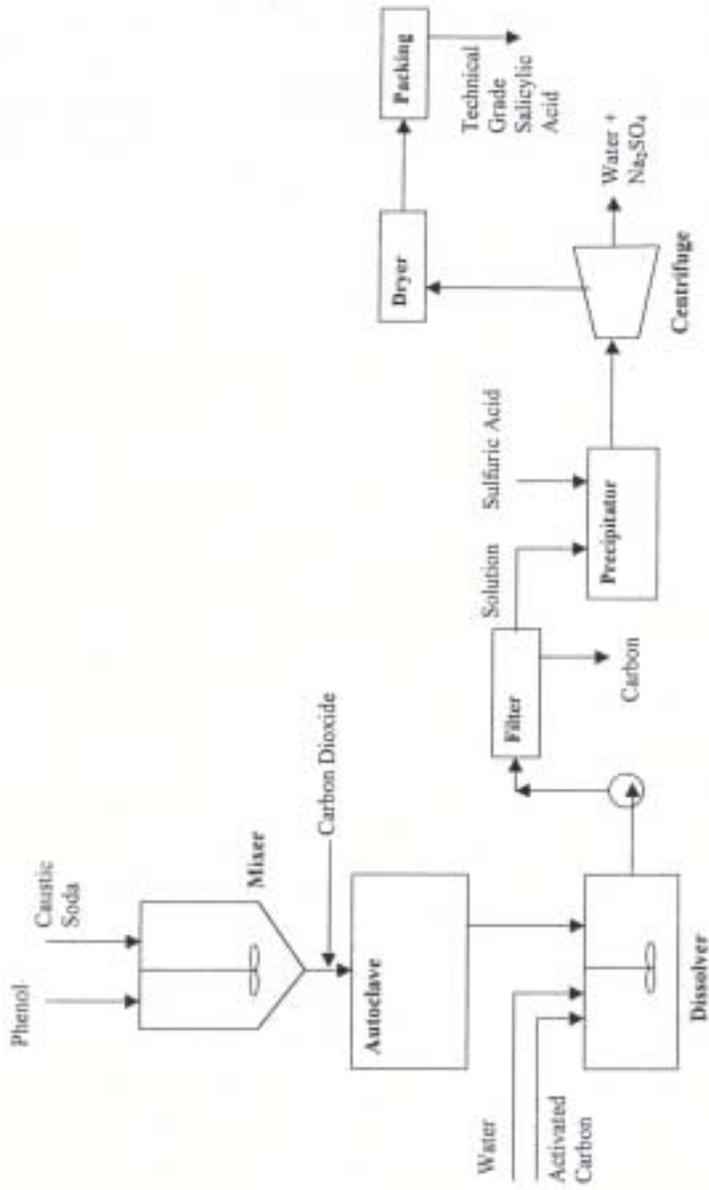


Figure 1: Manufacturing Process of Aspirin: Step 1 – Production of Salicylic Acid

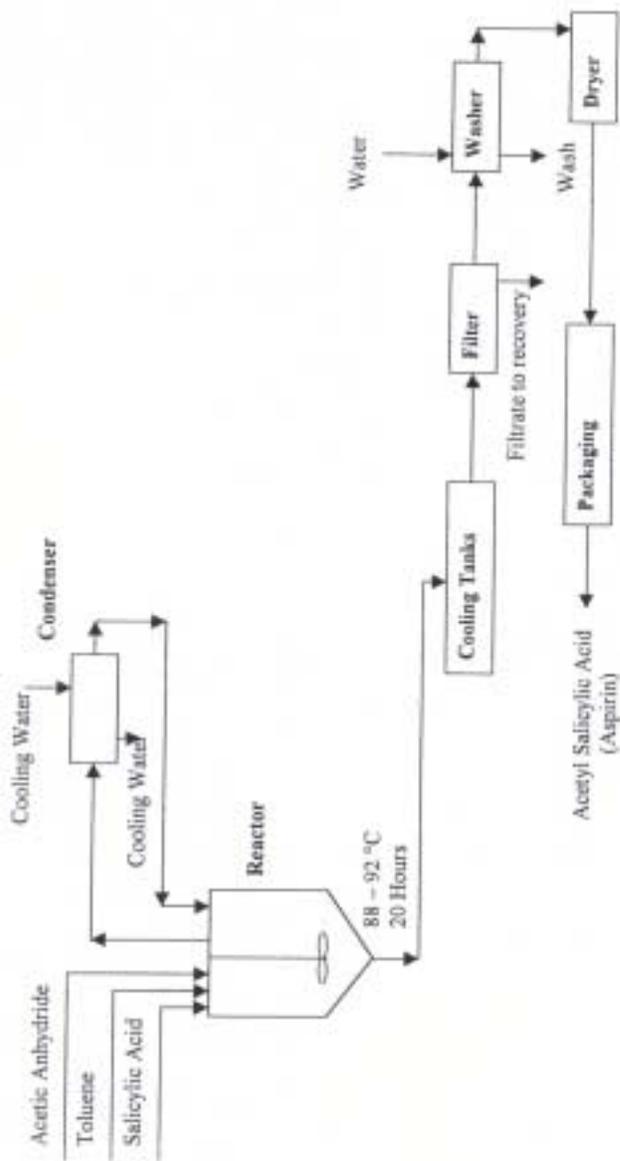


Figure 2: Manufacturing Process of Aspirin: Step II – Production of Acetylsalicylic Acid

4.4 Simplified Block Diagram to be Used For Material Balances.

Figure 3 and Figure 4 show the simplified block diagram for Steps I and II respectively. Block diagrams show the input and output of materials from the chemical process. You may wish to write the chemical reaction equations that take place within each block.

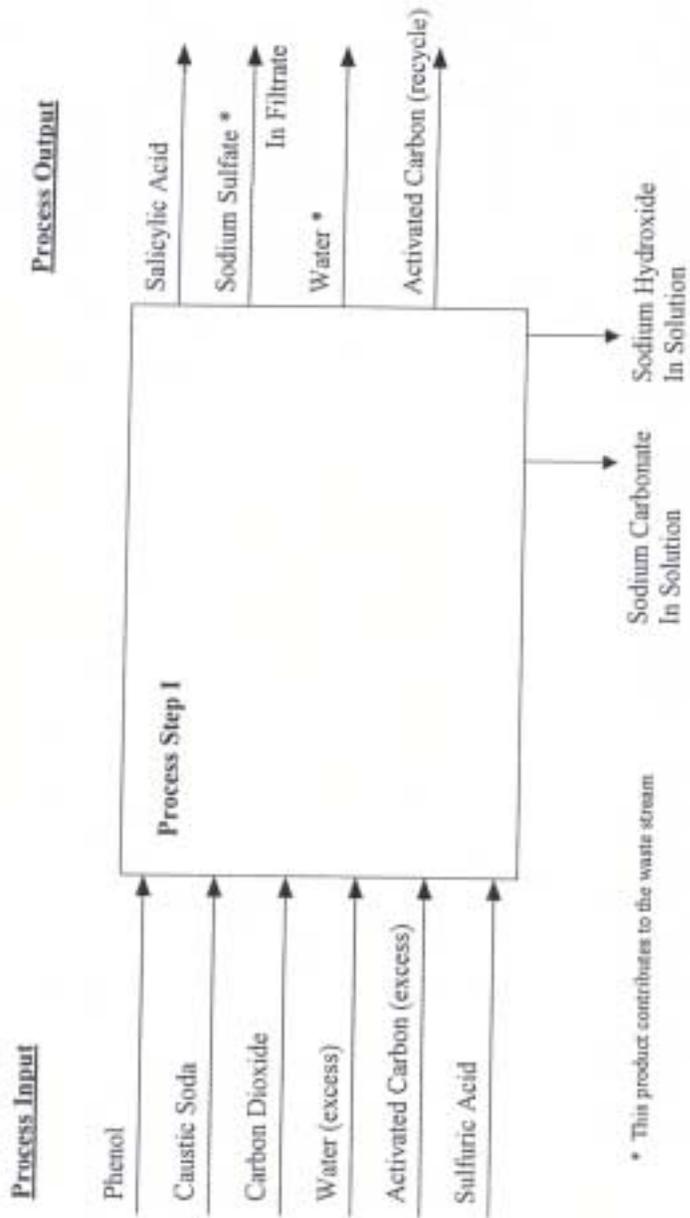


Figure 3: Manufacturing of Aspirin: Step 1 – Production of Salicylic Acid

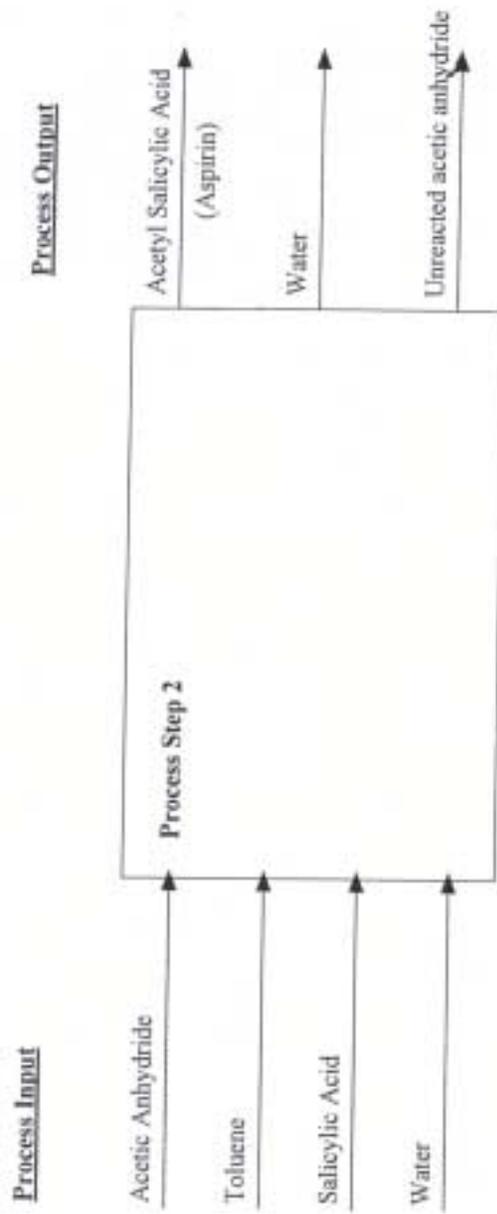


Figure 4: Manufacturing of Aspirin: Step II – Production of Acetylsalicylic Acid

5. The Problem

You, as a design team, are asked to design an aspirin production facility. The process capacity and the optimum location of a plant that must be designed depend upon many factors. Among these are:

1. Availability of raw materials.
2. Waste disposal problems (Pollution)
3. Amount of finished product that is needed in the projected market.
4. The share of this market that your plant can capture.
5. The projected year for which the design capacity is based.
6. The process yield and the process conversion for each step.

When all of these factors are combined, the design plant capacity can be calculated.

6. Estimation of Plant Capacity

The estimation of the plant capacity will depend upon the basis of calculations. For class uniformity, the following basis of calculation will be used.

Basis:

1. Design for Plant Capacity for 20 years into the future.
2. Step I
 - a. Process Conversion = 100% (Use 1% excess of Sodium Hydroxide and Carbon Dioxide)
 - b. Process yield = 99%
3. Step II
 - a. Process Conversion = 100%
 - b. Process yield = 99%
4. Market in United States
5. Assume excesses are very small and do not change stoichiometric relations

6.1 Calculation of Plant Capacity

One method that can be used to determine plant capacity in a given market is to determine the population and the per capita consumption because Aspirin is considered a mature growth product and depends upon population.

6.1.1 Population of United States

Prepare a Table based on literature data, showing the growth in the population of the United States. (Hint: The library would be a good place to begin your search for data.)

Table 1: Growth in Population of the United States

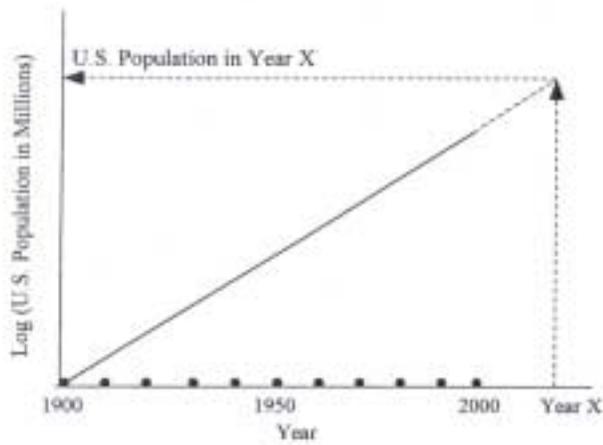
Year	Population
1900	
1910	
1920	
1930	
1940	
1950	
1960	
1970	
1980	
1990	
2000	

6.1.2 Population Projection into the Future

Growth curves can generally be linearized and linearly extrapolated a short distance for estimation purposes using a semi-logarithmic graph.

Prepare a semi-logarithmic graph showing the logarithmic U.S. population on the Y-axis and the year on the X-axis and extrapolate for twenty years into the future.

Figure 5: U.S. Population versus Year



An alternate method is to estimate the equation of the curve using available linear or curvilinear regression analysis and curve fit programs such as in EXCEL. Any curve can be curve fitted with a power series,

$$y = a + bx + cx^2 + dx^3 + \dots$$

The higher the power, the better the fit. In this case, use a quadratic curve fit.

$$y = a + bx + cx^2$$

or,

$$\log(U.S. Population) = a + b(\text{year}) + c(\text{year})^2$$

What is your equation?

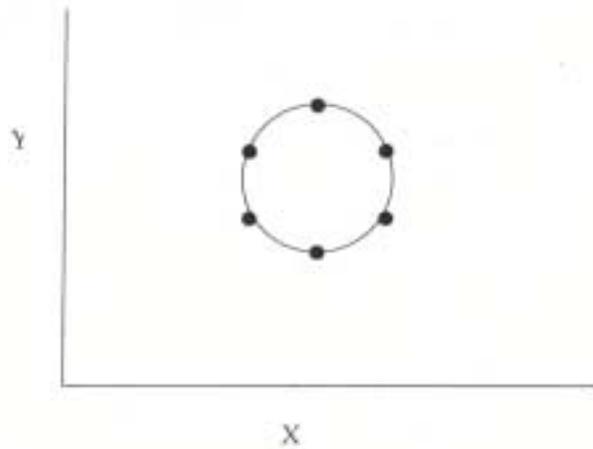
What are the values of the constants a, b, and c for the best curve and what are the units for a, b, and c?

$$\begin{aligned} a &= \underline{\hspace{2cm}} \\ b &= \underline{\hspace{2cm}} \\ c &= \underline{\hspace{2cm}} \end{aligned}$$

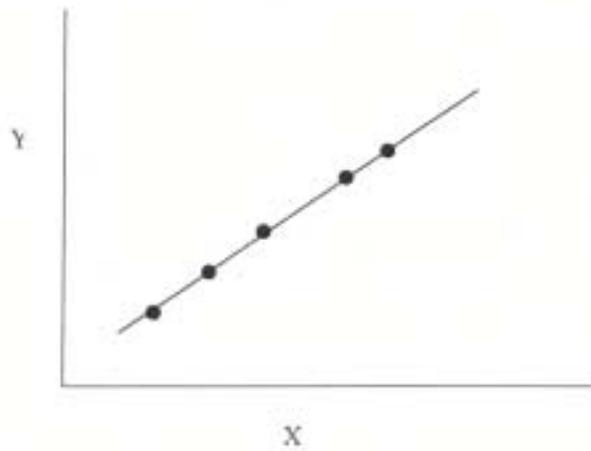
What is the statistical correlation coefficient, R^2 ?

$$R^2 = \underline{\hspace{2cm}}$$

The correlation coefficient measures the quality of your curve fit. If R^2 is zero, your data fall on a perfect circle or no correlation.



If $R^2 = 1$, the fit is a perfect straight line or curve fitting the data.



Is your approximation using a quadratic equation for curve fit adequate?

Do you feel that you need a cubic or higher power in the regression curve fit equation?

Compare your calculated projection of U.S. population for the 20 year projection using your regression equation with that from the linear extrapolation of the graph.

U.S. Population (calculated from Regression Equation)

U.S. Population (extrapolated from graph)

$$\text{Per Cent Difference} = \frac{\text{Calculated Value} - \text{Extrapolated Value}}{\text{Calculated Value}} \times 100$$

= _____

Which value do you have more confidence in?

What will be the U.S. population used in your design?

6.1.3 Estimate the Aspirin Requirements for the Projected Future

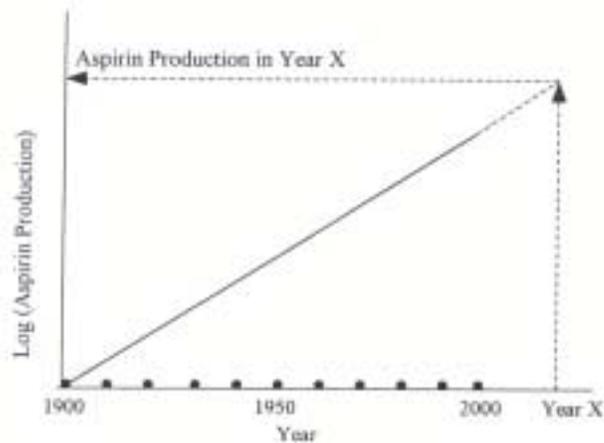
The procedure used for population can be used for Aspirin production rate.

Prepare a table based on literature values for Aspirin production.

Table 2: U.S. Aspirin Production

Year	Aspirin Produced, Pounds
1900	
1910	
1920	
1930	
1940	
1950	
1960	
1970	
1980	
1990	
2000	

Figure 6: U.S. Aspirin Production



$$y = a + bx + cx^2$$

$$\log(\text{U.S. Aspirin Production}) = a + b(\text{year}) + c(\text{year})^2$$

What is your equation?

What are the values of the constants a , b , and c for the best curve and what are the units for a , b , and c ?

$a =$ _____

$b =$ _____

$c =$ _____

What is the correlation coefficient, R^2 ?

$R^2 =$ _____

Compare your calculated projection of Aspirin production for the 20 year projection from the regression equation with that from the linear extrapolation of the graph.

U.S. Aspirin Production (calculated from Regression Equation)

_____ Pounds

U.S. Aspirin Production (extrapolated from graph)

_____ Pounds

$$\text{Per Cent Difference} = \frac{\text{Calculated Value} - \text{Extrapolated Value}}{\text{Calculated Value}} \times 100$$

= _____

Which value do you have more confidence in?

What will be the U.S. Aspirin production used in your design?

6.1.4 Alternate Estimate of the Aspirin Needs in 20 year projections

For any given year, determine the number of Aspirin tablets produced.

Year X = _____

Aspirin Produced = _____ pounds per year

U.S. Population = _____

In Year X

Aspirin Produced = _____ pounds / person per year

Per Person Per Year

U.S. Population = _____

In Year Y

Aspirin Needed In Year Y =

$$\frac{(\text{Aspirin Produced Per Person in Year X})}{(\text{U.S. Population in Year X})} \times (\text{U.S. Population in Year Y})$$

or,

$$\frac{\text{Aspirin Produced in Year X}}{\text{U.S. Population in Year X}} = \frac{\text{Aspirin Produced in Year Y}}{\text{U.S. Population in Year Y}}$$

6.1.5 Tablets of Aspirin Produced per year

Search the literature to determine the number of tablets made during that year.

Year X = _____

Tablets Made = _____

How many milligrams of Aspirin in one tablet?

_____ mg

How much Aspirin was made that year?

$$\frac{\text{Tablets}}{\text{tablet}} \times \frac{\text{mg}}{\text{mg}} \times \frac{1 \text{ g}}{1000 \text{ mg}} \times \frac{1 \text{ pound}}{454 \text{ g}} = \text{_____ pounds / year}$$

Use this number to compare with your projected production rate:

$$\frac{\text{Aspirin Produced in Year X}}{\text{U.S. Population in Year X}} = \frac{\text{Aspirin Produced in Year Y}}{\text{U.S. Population in Year Y}}$$

6.2 Design Basis

For 20 years in the future, how much Aspirin do you estimate will be needed in the U.S.?

_____ pounds / year

$$\frac{\text{pounds}}{\text{Year}} \left| \frac{454 \text{ g}}{1 \text{ pound}} \right| \frac{1 \text{ kg}}{1000 \text{ g}} = \text{_____ kilograms / year (kg/yr)}$$

What share of this market does market research show that you will be able to capture?

_____ Percent

What will be the Aspirin produced in your plant?

(Total U.S. Production in Year Y) (Fraction Of Market) = Aspirin Produced In Plant
Per Year

$$\frac{\text{kg}}{\text{yr.}} \quad | \quad \text{_____} \quad = \quad \text{_____ kg /yr.}$$

$$\quad \quad \quad \quad \quad \quad \quad \quad = \quad \text{_____ g /yr.}$$

**7. Determination of Raw Material Requirements and the Products
And By-Products Produced**

The estimation of the plant capacity will depend upon the basis of calculations. For class uniformity, the following basis of calculation will be used.

7.1.1 Using the Block Diagrams in Figure 3 and 4 and the chemical reactions for Steps I and II, list all chemicals entering and leaving the process.

7.1.2 Using the principles of stoichiometry learned in Chemistry, start with the acetyl salicylic acid (Aspirin) made in Step II based upon your plant capacity and calculate all of the materials entering and leaving each step of the process.

Hint: Don't forget to use the 99 percent yield for each process and the 1 percent excess sodium hydroxide and carbon dioxide added.

Table 3: Summary of Material Requirements to produce _____ kg /yr. Aspirin.

<u>Chemical</u>	<u>Amount Needed, kg/yr.</u>
-----------------	------------------------------

8. Pollution Abatement and Prevention

What are the waste products for your process?

How do you propose to handle this waste?

Suppose your process could not achieve 100 percent conversion, what other waste products would be made?

How would you dispose of these wastes?

Discuss what pollution abatement and pollution prevention technology you would use to alter your process in Figures 1 through 4.

9. Glossary of Terms

<i>Adsorption</i>	the adhesion of the molecules of a gas, liquid or dissolved substance on a surface of a solid
<i>Autoclave</i>	a closed vessel used for cooking, heating, etc. by using steam under pressure
<i>Centrifuge</i>	a machine, which uses the centrifugal force to separate solid particles of different densities
<i>Filtrate</i>	the liquid phase that passes through a filter
<i>Precipitate</i>	to cause a soluble substance to become insoluble and facilitate its separation
<i>Sublimation</i>	the direct conversion of a solid to a gas without first becoming a liquid

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11. Appendix

11.1 Obtain the Material Safety Data Sheets (MSDS) from the Internet for every chemical used in this process. (**Caution: Web pages can change for up-dating**)

I. Access the Chemical Abstract Service Number (CAS Number) for all chemicals used in your process.

1. Go to the Internet site

www.chemfinder.com

2. Hit **Enter**

3. Type in the name of the chemical in the space provided, for example, **Phenol**

4. Click on **Search**

5. Screen shows

Phenol [108-95-2]

6. Repeat steps 1-5 for each chemical used in the chemical process for the production of Aspirin.

II. Access the Material Safety Data Sheet (MSDS) for all chemicals used in your process.

1. Go to the Internet Site

www.ilpi.com/msds/index.html#internet

2. Role Screen and click on the desired Internet Site

For Example, role screen until you come to

msds on line

This site is adequate for your needs but you can use any of the others listed, for example,

Cornell

3. Type in the product name, for example, **Phenol**

4. Click on **Search, find it, etc.**

5. Many different compounds with phenol in them will appear but the compound **Phenol** is not shown

6. Role the screen to

ADD SELECTIONS TO MY LIST

7. Type in the CAS Number
8. Click on *Search*

Note: You will need a **Username** and a **Password**. You can access a free password, which will be sent to you via your e-mail address. You can change your password by following the directions.

9. When you have received your password, type your **Username** and **Password** in the spaces provided at the left of the screen.
10. Click on *Log-on*
11. Click on MSDS *Search*
12. Role the screen to

Product Name: Type in **Phenol**

CAS Number: Type in **108-95-2**

13. A table will appear with many different sources of **Phenol**
14. Click on the desired source of **Phenol** and/or under the **Plus**

column

to **Open MSDS**

15. Your Material Safety Data Sheet will appear on the screen for the chemical **Phenol**
16. Print your Material Safety Data Sheet
17. Repeat steps 1-16 for all of the chemicals used in the chemical Process to manufacture Aspirin