Chapter 2

Introduction to Process Design

2.0 OBJECTIVES

After studying this chapter, the reader should:

1. Understand the kinds of information gathered before designing a process to manufacture a chemical product.
2. Be able to implement the steps in creating flowsheets involving reactions, separations, and *T-P* change operations. Doing so identifies many alternatives that can be assembled into a synthesis tree containing the most promising alternatives.
3. Be aware of the major tasks in carrying out a process design with a guide to the sections and chapters of this textbook that cover methods for performing these tasks.
4. For the most promising *base-case* process flowsheets, know how to select the principal pieces of equipment and to create a detailed process flow diagram, with a material and energy balance table and a list of major equipment items.

2.1 INTRODUCTION

In process design, chemical engineers create chemical processes to convert raw materials into desired products, often identified using the product design strategies introduced in Chapter 1. In product design, the focus is on creating products that satisfy customer needs (i.e., the "voice of the customer"). Process design begins with well-defined chemical products, often available in prototype quantities from research laboratories. The process design team is challenged to design profitable processes that produce products in sufficient quantities and qualities to satisfy anticipated customer demands. Stated differently, the designers create potential processes to convert raw materials in specified states into a desired product(s) in a specified state(s).

Several key tasks/steps are involved in process design, most of which are carried out by design teams, but not necessarily in the same sequence. In this first process design chapter, these tasks are introduced, and illustrated in two principal examples, the intent being to provide introductory details while enabling readers to gain a broad appreciation of the typical approaches toward the design of manufacturing processes. For each task, references are made to subsequent chapters/sections in which more complete discussions are provided. Also, in areas where most chemical engineering students have learned techniques in earlier courses (e.g., thermodynamics, heat transfer, and separation processes), references are given and detailed methods are described later in this textbook. The first task normally involves information gathering, which is covered next.

Information Gathering

Process design problems are formulated in many ways, with many typical problem statements provided in Appendix II. Given a problem statement, usually a design group begins work to gather information that is the basis for its design. Often the project author is an excellent first source of information and data. But, in most cases, not all of the needed data are readily available, and guidance as to where to look or what assumptions are reasonable may be provided.

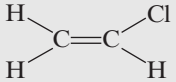
The data-gathering task usually involves searching the literature, especially the Internet for details about the chemical product to be manufactured. The designers need to know why the product is important. What are its uses? What are its characteristic properties? Who are the biggest producers (competitors)? For new products, much of this information is available from the product design team, which often participates on the team that designs its manufacturing process.

Gradually, the designers gain knowledge of the raw-material alternatives, and the principal chemical reactions, byproducts, and intermediates. Also, the designers begin to target a range of potential production levels and possible plant locations—usually making selections as the basis for their initial design work.

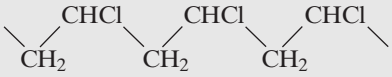
At this point, let's focus on the typical issues in designing a process to increase significantly the supply of a widely used commodity chemical, vinyl chloride. For this product, much information is readily available as provided in the problem statement that follows in Example 2.1.

EXAMPLE 2.1 ***Vinyl Chloride Manufacture—Information Gathering***

Consider the need to manufacture vinyl chloride,



a monomer intermediate for the production of polyvinyl chloride,



an important polymer (usually referred to just as vinyl) that is widely used for rigid plastic piping, fittings, and similar products. Over the years, large commercial plants have been built, some of which produce over 1 billion lb/yr. Hence, polyvinyl chloride and the monomer from which it is derived are referred to commonly as commodity chemicals that are produced continuously, rather than in batch, virtually everywhere. Historically, vinyl chloride was discovered in 1835 in the laboratory of the French chemist Regnault, and the first practical method for polymerizing vinyl chloride was developed in 1917 by the German chemists Klatte and Rollett (Leonard, 1971). Vinyl chloride is an extremely toxic substance and, therefore, industrial plants that manufacture it or process it must be designed carefully to satisfy government health and safety regulations.

An opportunity has arisen to satisfy a new demand, on the order of 800 million pounds per year, for vinyl-chloride monomer in a petrochemical complex on the Gulf Coast of the United States, given that an existing plant owned by the company produces 1 billion lb/yr of this commodity chemical. At this point, a design team has been formulated, and it has begun to consider four potential alternatives, including:

Alternative 1. A competitor's vinyl-chloride plant, which produces 2 MMM (billion) lb/yr of vinyl chloride and is located about 100 miles away, might be expanded to produce the required amount, which would be shipped by truck or rail in tank car quantities. In this case, the design team projects the purchase price and designs storage facilities. This might be the simplest solution to provide the monomer required to expand the local PVC plant.

Alternative 2. Chlorine from the electrolysis of NaCl solution could be processed and shipped by pipeline from a nearby plant. Then, chlorine could be reacted with in-house ethylene to produce the monomer and HCl as a byproduct.

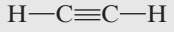
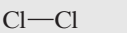
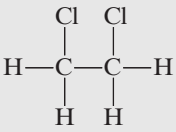
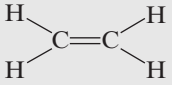
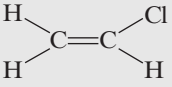
Alternative 3. Because the existing company petrochemical complex produces HCl as a byproduct in many processes (e.g., in chloroform and carbon tetrachloride manufacture) at a depressed price because large quantities are produced, HCl is normally available at low prices. Reactions of HCl with acetylene, or ethylene and oxygen, could produce 1,2-dichloroethane, an intermediate that can be cracked to produce vinyl chloride.

Alternative 4. Design an electrolysis plant to produce chlorine. One possibility is to electrolyze the HCl, available from within the petrochemical complex, to obtain H_2 and Cl_2. Then, chlorine could be reacted according to alternative 2. Elsewhere in the petrochemical complex, hydrogen could be reacted with nitrogen to form ammonia or with CO to produce methanol.

These are typical of the alternatives that might be selected from a large number of ideas that serve as a base on which to begin the process design. For this example, it's sufficient to consider only the production of the monomer with a focus on alternatives 2 and 3.

Data from chemistry laboratories focus on several promising chemical reactions involving the chemicals in Table 2.1. Thermophysical property data (e.g., normal boiling points, vapor pressures, heat capacities, latent heats of vaporization, heats of formation, and liquid densities) for these (and many other similar chemicals) are available in extensive databases (of the process simulators; see Chapter 7) and, when not available, can be estimated fairly reliably. The availability of toxicity, safety, and purchase price data is discussed following this example.

Table 2.1 Chemicals That Participate in Reactions to Produce Vinyl Chloride

Chemical	Molecular Weight	Chemical Formula	Chemical Structure
Acetylene	26.04	C_2H_2	
Chlorine	70.91	Cl_2	
1,2-Dichloroethane	98.96	$C_2H_4Cl_2$	
Ethylene	28.05	C_2H_4	
Hydrogen chloride	36.46	HCl	
Vinyl chloride	62.50	C_2H_3Cl	

Environmental and Safety Data

As mentioned in Section 3.4, design teams need toxicity data for raw materials, products, byproducts, and intermediates incorporated in a process design. In toxicology laboratories operated by chemical companies and governmental agencies, such as the U.S. Environmental Protection Agency (EPA) and the U.S. Food and Drug Administration (FDA), tests are run to check the effects of various chemicals on laboratory animals. The chemicals are administered in varying dosages, over differing periods, and in different concentrations, stimulating effects that are measured in many ways, including effects on the respiratory system, the skin, and the onset of cancer. In most cases, the results are provided in extensive reports or journal articles. In some cases, chemicals are difficult to classify as toxic or nontoxic.

Already it is well known that a number of common chemicals are toxic to humans and need to be avoided. One source of information on these chemicals is the Toxic Chemical Release Inventory (TRI), which is maintained by the U.S. EPA, and includes over 600 chemicals. A list of these chemicals is available at the Internet site:

http://www.epa.gov/tri/chemical/index.htm

Another source is provided by the ratings of the National Fire Protection Association (NFPA), which are tabulated for many chemicals in *Data for Process Design and Engineering Practice* (Woods, 1995). The first of three categories is titled "Hazard to Health" and entries are rated from 0 to 4, with 0 meaning harmless and 4 meaning extremely hazardous.

As seen in Table 3.2 and discussed in Section 3.5, data on the flammability of organic compounds are tabulated and, for those compounds not included in the table, methods are available to estimate the data. In addition, tables of flammability data are also available for aerosols and polymers in *Perry's Chemical Engineers' Handbook* (Green and Perry, 2008). The NFPA ratings provide a less quantitative source for many chemicals under "Flammability Hazard," which is the second of the three categories (also rated from 0 to 4).

Chemical Prices

Economics data are often related to supply and demand, and consequently they fluctuate and are much more difficult to estimate. Most companies, however, carry out market studies and have a basis for projecting market size and chemical prices. In view of the uncertainties, to be safe, economic analyses are often conducted using a range of chemical prices to determine the sensitivity of the results to specific prices.

One widely used source of prices of commodity chemicals is from *ICIS Chemical Business* (formerly *Chemical Market Reporter*), a weekly publication. Their Web site, http://www.icis.com/StaticPages/Students.htm, provides information for students in their Knowledge Zone. It should be noted, however, that these prices may not reflect the market situation in a particular location; nevertheless, they provide a good starting point. In addition, commodity chemical prices may be found via ICIS pricing. This service publishes weekly pricing benchmarks to the industry and offers samples of reports that are approximately six months old via the following link: http://www.icispricing.com/il_shared/il_splash/chemicals.asp?llink%. Obviously, to obtain better estimates, at least for the immediate future, the manufacturers of the chemicals should be contacted directly. Lower prices than those listed can be negotiated. Subscribers to *ICIS Chemical Business* can also obtain more recent market trends and data derived from both their ICIS news and ICIS pricing services.

In some cases, it may be desirable to estimate the prices of utilities, such as steam, cooling water, and electricity, during process creation. Here also, appropriate prices can be obtained from local utility companies. As a start, however, values are often tabulated, as provided in Table 17.1.

Summary

To the extent possible using the literature, company files, computer data banks, and similar sources, the design team assembles a preliminary database for use in preliminary process synthesis, the subject of Section 2.3. Typically, the database contains thermophysical property data, rudimentary reaction-rate data, data concerning toxicity and flammability of the chemicals, and chemical prices. In cases where data cannot be located, estimation methods are often available. However, when the results are sensitive to the estimates, conclusions must be drawn with caution. In most cases, when a process looks promising, an experimental program is initiated, as discussed in the next section. Note that other kinds of data are normally not necessary until the detailed process flow diagram has been developed for the base-case design, and the design team is preparing to complete the detailed design of the equipment items. Note also that when molecular-structure design has been used to select the chemical product, experimental data and/or theoretical estimates are usually available in data banks, especially in drug development.

2.2 EXPERIMENTS

Many design concepts are the result of extensive experiments in the laboratory, which provide valuable data for the design team. Often, however, laboratory experiments are carried out in small vessels, using small quantities of expensive solvents, and under conditions where the conversion and selectivity to the desired product are far from optimal. For this reason, as a design concept becomes more attractive, it is common for the design team to request additional experiments at other conditions of compositions, temperatures, and pressures, and using solvents that are more representative of those suitable for large-scale production. In cases where no previous in-house experimental work has been done, laboratory programs are often initiated at the request of the design team, especially when estimates of the rates of reaction are not very reliable. When chemical reactions involve the use of catalysts, it is essential that experiments be conducted on catalyst life using feedstocks that are representative of those to be used for large-scale production, and that may contain potential catalyst poisons.

Laboratory experiments may also be necessary to aid in the selection and preliminary design of separation operations. The separation of gas mixtures requires consideration of absorption, adsorption, and gas permeation, all of which may require the search for an adequate absorbent, adsorbent, and membrane material, respectively. When nonideal liquid mixtures are to be separated, laboratory distillation experiments should be conducted early because the possibility of azeotrope formation can greatly complicate the selection of adequate separation equipment, which may involve the testing of one or more solvents or entrainers. When solids are involved, early laboratory tests of such operations as crystallization, filtration, and drying are essential.

Clearly, as data are obtained in the laboratory, they are tabulated and usually regressed, to allow addition to the preliminary database for use by the design team in preliminary process synthesis, which is the subject of the next section.

2.3 PRELIMINARY PROCESS SYNTHESIS

Having gathered information and carried out experiments, if necessary, a process design team is prepared to create an initial process flowsheet to convert the potential raw materials into chemical products. Various processing operations are used to carry out chemical reactions and to separate products and byproducts from each other and from unreacted raw materials. The assembly of these operations into a process flowsheet is known as *process synthesis*. In many respects, one of the greatest challenges in process design involves the synthesis of configurations that produce chemicals in a reliable, safe, and economical manner, at high yield and with little or no waste.

Chemical State

To initiate process synthesis, the design team must decide on raw materials, products, and byproducts specifications. These are referred to as *states*. Note that the state selections can be changed later with modifications to the flowsheets. To define the state, values of the following conditions are needed:

1. Mass (flow rate)
2. Composition (mole or mass fraction of each chemical species of a unique molecular type)
3. Phase (solid, liquid, or gas)
4. Form, if solid phase (e.g., particle size distribution and particle shape)
5. Temperature
6. Pressure

In addition, some well-defined properties, such as the intrinsic viscosity, average molecular weight, color, and odor of a polymer, may be required. These are often defined in connection with the research and marketing departments, which work to satisfy the requests and requirements of their customers. It is not uncommon for a range of conditions and properties to be desired, some of which are needed intermittently by various customers as their downstream requirements vary. When this is the case, care must be taken to design a process that is sufficiently flexible to meet changing demands.

For most chemicals, the scale (i.e., production level or flowrate) of the process is a primary consideration early in the design process. Working together with the marketing people, the scale of the process is determined on the basis of the projected demand for the product. Often the demographics of the most promising customers have an important impact on the location of the plant and the choice of its raw materials. As the scale and the location are established, the composition, phase, form, temperature, and pressure of each product and raw-material stream are considered as well. When the desired states of these streams have been identified, the problem of process synthesis becomes better defined. As shown in Figure 2.1, for the production of vinyl chloride, it remains to insert the process operations into the flowsheet.

It is noteworthy that once the state of a substance is fixed by conditions 1–6, all physical properties (except for the form of a solid), including viscosity, thermal conductivity, color, refractive index, and density, take on definite values. Furthermore, the state of a substance is independent of its position in a gravitational field and its velocity. Although there are other conditions (magnetic field strength, surface area) whose values are needed under certain conditions, the six conditions listed above are usually sufficient to fix the state of a substance.

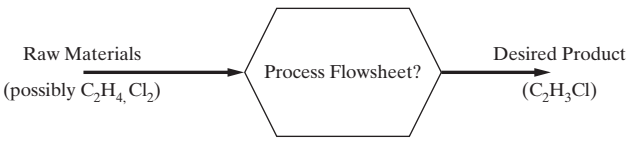


Figure 2.1 Process synthesis problem.

Process Operations

Throughout the chemical engineering literature, many kinds of equipment, so-called *unit operations*, are described, including distillation columns, absorbers, strippers, evaporators, decanters, heat exchangers, filters, and centrifuges, just to mention a few. The members of this large collection all involve one or more of these basic operations:

1. Chemical reaction
2. Separation of chemical mixtures
3. Phase separation
4. Change of temperature
5. Change of pressure
6. Change of phase
7. Mixing and splitting of streams or batches
8. Operations on solids, such as size reduction and enlargement

Since these are the building blocks of nearly all chemical processes, it is common to create flowsheets involving these basic operations as a first step in process synthesis. Then, in a *task integration* step, operations are combined where feasible. In the remainder of this section, each of the basic operations is considered in some detail before considering the steps in process synthesis.

Chemical Reaction Operations

Chemical reaction operations are at the heart of many chemical processes. They are inserted into a flowsheet to effect differences in the molecular types between raw-material and product streams. To this end, they involve the chemistry of electron transfers, free-radical exchanges, and other reaction mechanisms, to convert the molecular types of the raw materials into products of other molecular types that have the properties sought by a company's customers. Clearly, the positioning of the reaction operations in the flowsheet involves many considerations, including the degree of conversion, reaction rates, competing side reactions, and the existence of reactions in the reverse direction (which can result in constraints on the conversion at equilibrium). These, in turn, are related closely to the temperature and pressure at which the reactions are carried out, the methods for removing or supplying energy, and the catalysts that provide competitive reaction rates and selectivity to the desired products.

Separation Operations

Separation operations appear in almost every process flowsheet. They are needed whenever there is a difference between the desired composition of a product or an intermediate stream and the composition of its source, which is either a feed or an intermediate stream. Separation operations are inserted when the raw materials contain impurities that need to be removed before further processing, such as in reactors, and when products, byproducts, and unreacted raw materials coexist in a reactor effluent stream. The choice of separation operations depends first on the phase of the mixture and second on the differences in the physical properties of the chemical species involved. For liquid

mixtures, when differences in volatilities (i.e., vapor pressure) are large, it is common to use vapor–liquid separation operations (e.g., distillation), which are by far the most common. For some liquid mixtures, the melting points differ significantly and solid–liquid separations, involving crystallization, gain favor. When differences in volatilities and melting points are small, it may be possible to find a solvent that is selective for some components but not others, and to use a liquid–liquid separation operation. For other mixtures, particularly gases, differences in absorbability (in an absorbent), adsorbability (on an adsorbent; e.g., activated carbon, molecular sieves, or zeolites), or permeability through a membrane may be exploited with adsorption and membrane separation operations.

Temperature Change Operations

The need to change temperatures usually occurs throughout a chemical process. In other words, there are often differences in the temperatures of the streams that enter or leave the process or that enter or leave adjacent process operations, such as reaction and separation operations. Often a process stream needs to be heated or cooled from its *source* temperature to its *target* temperature. This is best accomplished through heat exchange with other process streams that have complementary cooling and heating demands.

Pressure Change Operations

The positioning of pressure-change operations such as gas compressors, gas turbines or expanders, liquid pumps, and pressure-reduction valves in a process flowsheet is often ignored in the early stages of process design. As will be seen, it is common to select the pressure levels for reaction and separation operations. When this is done, pressure-change operations will be needed to decrease or increase the pressure of the feed to the particular operation. In fact, for processes that have high power demands, usually for gas compression, there is often an opportunity to obtain much of the power through integration with a source of power, such as turbines or expanders, which are pressure-reduction devices. In process synthesis, however, where alternative process operations are being assembled into flowsheets, it has been common to disregard the pressure drops in pipelines when they are small relative to the pressure level of the process equipment. Liquid pumps to overcome pressure drops in lines and across control valves and to elevate liquid streams to reactor and column entries often have negligible costs. Increasingly, as designers recognize the advantages of considering the controllability of a potential process while developing the base-case design, the estimation of pressure drops gains importance because flow rates are controlled by adjusting the pressure drop across a valve.

Phase Change Operations

Often there are significant differences in the phases that exit from one process operation and enter another. For example, hot effluent gases from a reactor are condensed, or partially condensed, often before entering a separation operation, such as a vapor–liquid separator (e.g., a flash vessel or a distillation tower). In process synthesis, it is common to position a phase-change operation using temperature- and/or pressure-reduction operations, such as heat exchangers and valves.

Mixing Operations

The mixing operation is often necessary to combine two or more streams and is inserted when chemicals are recycled and when it is necessary to blend two or more streams to achieve a product specification.

Synthesis Steps

Given the states of the raw-material and product streams, process synthesis involves the selection of processing operations to convert the raw materials into products. In other words, each operation can be viewed as having a role in eliminating one or more of the property differences between the raw materials and the desired products. As each operation is inserted into a flowsheet, the effluent streams from the new operation are closer to those of the required products. For example, when a reaction operation is inserted, the stream leaving often has the desired molecular types, but not the required composition, temperature, pressure, and phase. To eliminate the remaining differences, additional operations are needed. As separation operations are inserted, followed by operations to change the temperature, pressure, and phase, fewer differences remain. In one parlance, the operations are inserted with the goal of reducing the differences until the streams leaving the last operation are identical in state to the required products. Formal, logic-based strategies, involving the proof of theorems that assert that all of the differences have been eliminated, have been referred to as *means–end analysis*. In process synthesis, these formal strategies have not been developed beyond the synthesis of simple processes. Rather, an informal approach, introduced by Rudd, Powers, and Siirola (1973) in a book entitled *Process Synthesis*, has been adopted widely. It involves positioning the process operations in the following steps to eliminate the differences:

Synthesis Step	Process Operations
1. Eliminate differences in molecular types	Chemical reactions
2. Distribute the chemicals by matching *sources* and *sinks*	Mixing
3. Eliminate differences in composition	Separation
4. Eliminate differences in temperature, pressure, and phase	Temperature, pressure, and phase change
5. Integrate tasks; that is, combine operations into *unit processes* and decide between continuous and batch processing	

Rather than discuss these steps in general, it is preferable to examine how they are applied for synthesis of a vinyl-chloride process as will be shown in Example 2.2.

Continuous or Batch Processing

When selecting processing equipment in the task-integration step, the production scale strongly impacts the operating mode. For the production of commodity chemicals, large-scale continuous processing units are selected, whereas for the production of many specialty chemicals as well as industrial and configured consumer chemical products, small-scale batch processing units are preferable. A key decision is the choice between continuous, or batch, or possibly semicontinuous operation.

Commodity Chemicals

In this subsection, an example is presented to synthesize a process for manufacture of a typical commodity chemical, vinyl chloride. See Example 2.3 for a discussion of process synthesis of a batch process to manufacture the pharmaceutical, tissue-plasminogen activator (tPA).

EXAMPLE 2.2 ***Process Synthesis of a Vinyl-Chloride Process***

Following the Process Synthesis Steps 1–5, a process flowsheet to manufacture vinyl chloride is synthesized in this example. Note that some assistance was provided by two patents (Benedict, 1960; B. F. Goodrich Co., 1963). Often, similar patents, located by design teams when gathering information, provide considerable help during process synthesis.

Step 1 Eliminate Differences in Molecular Type: For the manufacture of vinyl chloride, data from the chemistry laboratory focus on several promising chemical reactions involving the chemicals shown in Table 2.1. Note that since vinyl chloride has been a commodity chemical for many years, these chemicals and the reactions involving them are well known. For newer substances, the design team often begins to carry out process synthesis as the data are emerging from the laboratory. The challenge, in these cases, is to guide the chemists away from those reaction paths that lead to processes that are costly to build and operate, and to arrive at designs as quickly as possible, in time to capture the market before a competitive process or chemical is developed by another company.

Returning to the manufacture of vinyl chloride, the principal reaction pathways are as follows.

1. ***Direct Chlorination of Ethylene***

$$C_2H_4 + Cl_2 \rightarrow C_2H_3Cl + HCl \qquad (2.1)$$

This reaction appears to be an attractive solution to design alternative 2. It occurs spontaneously at a few hundred degrees Celsius, but unfortunately does not give a high yield of vinyl chloride without simultaneously producing large amounts of byproducts such as dichloroethylene. Another disadvantage is that one of the two atoms of expensive chlorine is consumed to produce the byproduct hydrogen chloride, which may not be sold easily.

2. ***Hydrochlorination of Acetylene***

$$C_2H_2 + HCl \rightarrow C_2H_3Cl \qquad (2.2)$$

This exothermic reaction is a potential solution for the concept denoted as alternative 3. It provides a good conversion (98%) of acetylene to vinyl chloride at 150°C in the presence of mercuric chloride ($HgCl_2$) catalyst impregnated in activated carbon at atmospheric pressure. These are fairly moderate reaction conditions, and hence, this reaction deserves further study.

3. ***Thermal Cracking of Dichloroethane from Chlorination of Ethylene***

$$C_2H_4 + Cl_2 \rightarrow C_2H_4Cl_2 \qquad (2.3)$$

$$C_2H_4Cl_2 \rightarrow C_2H_3Cl + HCl \qquad (2.4)$$

$$C_2H_4 + Cl_2 \rightarrow C_2H_3Cl + HCl \quad \text{(overall)} \qquad (2.1)$$

The sum of reactions (2.3) and (2.4) is equal to reaction (2.1). This two-step reaction path has the advantage that the conversion of ethylene to 1,2-dichloroethane in exothermic reaction (2.3) is about 98% at 90°C and 1 atm with a Friedel–Crafts catalyst such as ferric chloride ($FeCl_3$). Then, the dichloroethane intermediate is converted to vinyl chloride by thermal cracking according to the endothermic reaction (2.4), which occurs spontaneously at 500°C and has conversions as high as 65%. The overall reaction presumes that the unreacted dichloroethane is recovered entirely from the vinyl chloride and hydrogen chloride and recycled. This reaction path has the advantage that it does not produce dichloroethylene in significant quantities, but it shares the disadvantage with reaction path 1 of producing HCl. It deserves further examination as a solution to design alternative 2.

4. ***Thermal Cracking of Dichloroethane from Oxychlorination of Ethylene***

$$C_2H_4 + 2HCl + \frac{1}{2}O_2 \rightarrow C_2H_4Cl_2 + H_2O \qquad (2.5)$$

$$C_2H_4Cl_2 \rightarrow C_2H_3Cl + HCl \qquad (2.4)$$

$$C_2H_4 + HCl + \frac{1}{2}O_2 \rightarrow C_2H_3Cl + H_2O$$

$$\text{(overall)} \qquad (2.6)$$

In reaction (2.5), which *oxychlorinates* ethylene to produce 1,2-dichloroethane, HCl is the source of chlorine. This highly exothermic reaction achieves a 95% conversion of ethylene to dichloroethane at 250°C in the presence of cupric chloride ($CuCl_2$) catalyst, and is an excellent candidate when the cost of HCl is low. As in reaction path 3, the dichloroethane is cracked to vinyl chloride in a pyrolysis step. This reaction path should be considered also as a solution for design alternative 3.

5. ***Balanced Process for Chlorination of Ethylene***

$$C_2H_4 + Cl_2 \rightarrow C_2H_4Cl_2 \qquad (2.3)$$

$$C_2H_4 + 2HCl + \frac{1}{2}O_2 \rightarrow C_2H_4Cl_2 + H_2O \qquad (2.5)$$

$$2C_2H_4Cl_2 \rightarrow 2C_2H_3Cl + 2HCl \qquad (2.4)$$

$$2C_2H_4 + Cl_2 + \frac{1}{2}O_2 \rightarrow 2C_2H_3Cl + H_2O$$

$$\text{(overall)} \qquad (2.7)$$

Table 2.2 Assumed Cost of Chemicals Purchased or Sold in Bulk Quantities

Chemical	Cost (cents/lb)
Ethylene	30
Acetylene	80
Chlorine	18
Vinyl chloride	35
Hydrogen chloride	25
Water	0
Oxygen (air)	0

This reaction path combines paths 3 and 4. It has the advantage of converting both atoms of the chlorine molecule to vinyl chloride. All of the HCl produced in the pyrolysis reaction is consumed in the oxychlorination reaction. Indeed, it is a fine candidate for the solution of design alternative 2.

Given this information, it seems clear that the design team would reject reaction path 1 on the basis of its low *selectivity* with respect to the competing reactions (not shown) that produce undesirable byproducts. This leaves the other reaction paths as potentially attractive to be screened on the basis of the chemical prices. Although it is too early to estimate the cost of the equipment and its operation before the remaining process operations are in place, the design team normally computes the *economic potential*, *EP* (i.e., the sales minus the cost of raw materials, not including the cost of utilities and operating costs) for each reaction path and uses it as a vehicle for screening out those that cannot be profitable. To illustrate this process for the production of vinyl chloride, Table 2.2 provides a representative set of prices for the principal chemicals, obtained from a source such as the ICIS Business Americas (formerly the *Chemical Marketing Reporter*), as discussed earlier.

The economic potential is computed by first converting to a mass basis, as illustrated for reaction path 3:

	C_2H_4	+ Cl_2	= C_2H_3Cl	+ HCl
lbmol	1	1	1	1
Molecular weight	28.05	70.91	62.50	36.46
lb	28.05	70.91	62.50	36.46
lb/lb of vinyl chloride	0.449	1.134	1	0.583
cents/lb	30	18	35	25

Then, the economic potential is $35(1) + 25(0.583) - 30(0.449) - 18(1.134) = 15.69$ cents/lb of vinyl chloride. Similar estimates are made for the overall reaction in each of the reaction paths, it being assumed that complete conversion can be achieved without any side reactions (not shown), with the results shown in Table 2.3.

Even without the capital costs (for construction of the plant, purchase of land, etc.) and the operating costs (for labor, steam, electricity, etc.), the economic potential for reaction path 2 is negative, whereas the economic potentials for the other reaction paths are positive. This is principally because acetylene is very expensive relative to ethylene. The fairly high price of HCl also contributes to the inevitable conclusion that vinyl chloride cannot be produced profitably using this reaction path. It should be noted that the price of HCl is often very sensitive to its availability in a petrochemical complex. In some situations, it may be available in large quantities as a byproduct from another process at very low cost. At a much lower price, reaction path 2 would have a positive economic potential, but would not be worthy of further consideration when compared with the three reaction paths involving ethylene. Turning to these paths, all have sufficiently positive economic potentials, and hence are worthy of further consideration. It is noted that the price of HCl strongly influences the economic potentials of reaction paths 3 and 4, with the economic potential of reaction path 5 midway between the two. Before proceeding with the synthesis, the design team would be advised to examine how the economic potentials vary with the price of HCl.

Table 2.3 Economic Potential for Production of Vinyl Chloride (Based on Chemical Prices in Table 2.2)

Reaction Path	Overall Reaction	Economic Potential (cents/lb of vinyl chloride)
2	$C_2H_2 + HCl = C_2H_3C1$	−16.00
3	$C_2H_4 + Cl_2 = C_2H_3Cl + HCl$	15.69
4	$C_2H_4 + HCl + \frac{1}{2}O_2 = C_2H_3C1 + H_2O$	6.96
5	$2C_2H_4 + Cl_2 + \frac{1}{2}O_2 = 2C_2H_3C1 + H_2O$	11.32

Figure 2.2 shows the first step toward creating a process flowsheet for reaction path 3. Each reaction operation is positioned with arrows representing its feed and product chemicals. The *sources* and *sinks* are not shown because they depend on the *distribution of chemicals*, the next step in process synthesis. The flow rates of the external sources and sinks are computed assuming that the ethylene and chlorine sources are converted completely to the vinyl chloride and hydrogen chloride sinks. Here, a key decision is necessary to set the scale of the process, that is, the production rate at capacity. In this case, a capacity of 100,000 lb/hr (~800 million lb/yr, assuming operation 330 days annually—an operating factor of 0.904) is dictated by the opportunity presented above. Given this flow rate for the product (principal sink for the process), the flow rates of the HCl sink and the raw-material sources can be computed by assuming that the raw materials are converted to the products according to the overall reaction. Any unreacted raw materials are separated from the reaction products and recycled. By material balance, the results in Figure 2.2 are obtained, where each flow rate in lbmol/hr is 1,600.

Similar flowsheets, containing the reaction operations for reaction paths 4 and 5, would be prepared to complete Step 1 of the synthesis. These are represented in the synthesis tree in Figure 2.7, which will be discussed after all of the synthesis steps have been completed. Note that their flowsheets are not included here due to space limitations, but are requested in Exercise 2.5 at the end of the chapter. As the next steps in the synthesis are completed for reaction path 3, keep in mind that they would be carried out for the other reaction paths as well. Note, also, that only the most promising flowsheets are developed in detail, usually by an expanded design team or, in some cases, by a competitive design team.

Step 2 Distribute the Chemicals: In Step 2, where possible, the sources and sinks for each of the chemical species in Figure 2.2 are matched so that the total mass flow into a reactor equals the total mass flow out. This often entails the introduction of mixing operations to eliminate differences in flow rates when a single sink is supplied by two or more sources. In other cases, a single source is divided among several sinks. To achieve the distribution of chemicals in Figure 2.3, the ethylene and chlorine sources are matched with their sinks into the chlorination reactor. It is assumed that ethylene and chlorine enter the reactor in the stoichiometric ratio of 1:1 as in reaction (2.3). Because the raw materials are in this ratio, no differences exist between the flow rates of the sources and sinks, and hence, no mixers are needed. Flow rates of 113,400 lb/hr of chlorine and 44,900 lb/hr of ethylene produce 158,300 lb/hr of dichloroethane. When it is desired to have an excess of one chemical in relation to the other so as to completely consume the other chemical, which may be toxic or very expensive (e.g., Cl_2), the other raw material (e.g., C_2H_4) is mixed with recycle and fed to the reactor in excess. For example, if the reactor effluent contains unreacted C_2H_4, it is separated from the dichloroethane product and recycled to the reaction operation. Note that the recycle is the source of the excess chemical, and the flow rate of the external source of C_2H_4 for a given production rate of dichloroethane is unaffected. This alternative distribution of chemicals is discussed further in Section 6.3 and illustrated in Figure 6.1. Returning to the distribution of chemicals in Figure 2.3, note that, at reactor conditions of 90°C and 1.5 atm, experimental data indicate that 98% of the ethylene is converted to dichloroethane, with the remainder converted to unwanted byproducts such as trichloroethane. This loss of yield of main product and small fraction of byproduct is neglected at this stage in the synthesis.

Next, the dichloroethane source from the chlorination operation is sent to its sink in the pyrolysis operation, which operates at 500°C. Here only 60% of the dichloroethane is converted to vinyl chloride with a byproduct of HCl, according to reaction (2.4). This conversion is within the 65% conversion claimed in the patent. To satisfy the overall material balance, 158,300 lb/hr of dichloroethane must produce 100,000 lb/hr of vinyl chloride and 58,300 lb/hr of HCl. But a 60% conversion produces only 60,000 lb/hr of vinyl chloride. The additional dichloroethane needed is computed by mass balance to equal $[(1 - 0.6)/0.6] \times 158{,}300$ or 105,500 lb/hr. Its source is a recycle stream from the separation of vinyl chloride from unreacted dichloroethane, from a mixing operation inserted to combine the two sources, to give a total of 263,800 lb/hr. The effluent stream from the pyrolysis operation is the source for the vinyl-chloride product, the HCl byproduct, and the dichloroethane recycle. To enable these chemicals to be supplied to their sinks, one or more separation operations are needed and are addressed in the next synthesis step.

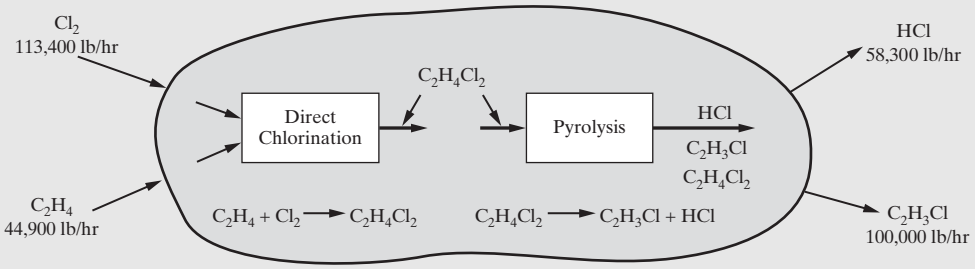


Figure 2.2 Reaction operations for the thermal cracking of dichloroethane from the chlorination of ethylene (reaction path 3)

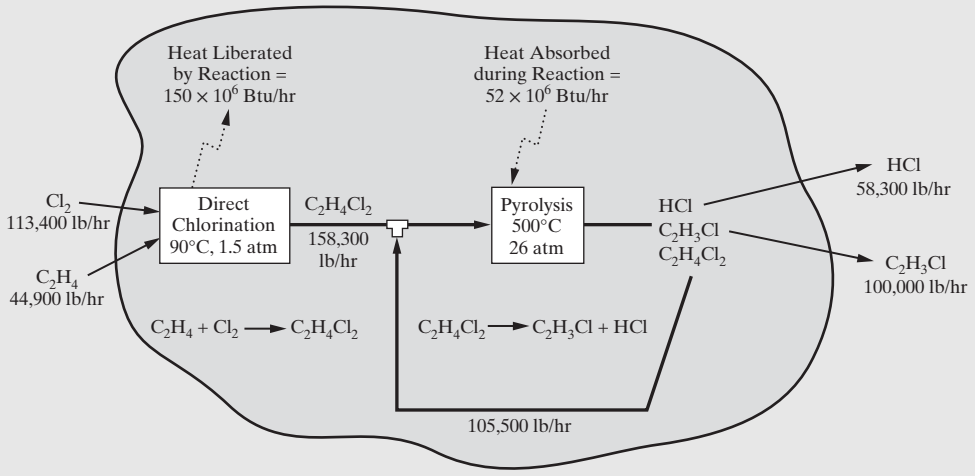


Figure 2.3 Flowsheet showing a distribution of chemicals for thermal cracking of dichloroethane from chlorination of ethylene (reaction path 3).

SUB-EXAMPLE 2.2.1 Pyrolysis Recycle Mass Balance

Assume that only 40% of the dichloroethane is converted to vinyl chloride in the pyrolysis operation. Estimate the recycle flow rate, assuming a perfect separation of dichloroethane from the pyrolysis effluent.

SOLUTION

Mass balance for dichloroethane:

$$(158{,}300 + R) \times 0.6 = R$$

Solving for R:

$$(1 - 0.6) \times R = 158{,}300 \times 0.6 = 94{,}980 \text{ lb/hr}$$

$$R = 94{,}980/0.4 = 237{,}450 \text{ lb/hr}$$

Figure 2.3 also shows the heats of reaction for the two reaction steps. These are computed at the temperatures and pressures of the reaction operations from heats of formation and heat capacities as a function of temperature. There are many sources of these data, especially the process simulators that are discussed in Chapter 7. When a simulator, such as ASPEN PLUS, is used, it is convenient to define each of the reaction operations and to perform an energy balance at reactor conditions. The simulators report the rate at which heat must be transferred to or from the reactor to achieve exit conditions from given inlet conditions or, if operated adiabatically, the exit conditions for no heat transfer, as discussed on the multimedia modules, which can be downloaded from the Wiley Web site associated with this book; follow the paths, *ASPEN → Chemical Reactors and HYSYS → Chemical Reactors*. For reaction path 3, the chlorination operation provides a large source of energy, 150 million Btu/hr, but at a low temperature, 90°C, whereas the pyrolysis operation requires much less energy, 52 million Btu/hr, at an elevated temperature, 500°C. Since this heat source cannot be used to provide the energy for pyrolysis, other uses for this energy should be sought as the synthesis proceeds. These and other sources and sinks for energy are considered during task integration in Step 5.

As for the pressure levels in the reaction operations, 1.5 atm is selected for the chlorination reaction to prevent the leakage of air into the reactor to be installed in the task-integration step. At atmospheric pressure, air might leak into the reactor and build up in sufficiently large concentrations to exceed the flammability limit. For the pyrolysis operation, 26 atm is recommended by the B.F. Goodrich patent (1963) without any justification. Since the reaction is irreversible, the elevated pressure does not adversely affect the conversion. Most likely, the patent recommends this pressure to increase the rate of reaction and, thus, reduce the size of the pyrolysis furnace, although the tube walls must be thick and many precautions are necessary for operation at elevated pressures. The pressure level is also an important consideration in selecting the separation operations, as will be discussed in the next synthesis step.

Referring to Figure 2.7, at the "Distributions of Chemicals" level, two branches have been added to the synthesis tree to represent the two distributions in connection with reaction path 3. Each of these branches represents a different partially completed flowsheet, that is, Figures 2.3 and 6.1. Other distributions arise in connection with reaction paths 4 and 5. These are represented using dashed lines in the synthesis tree.

Step 3 Eliminate Differences in Composition: As mentioned earlier, for each distribution of chemicals, the needs for separation become obvious. In Figure 2.3, for example, it is clear that the pure effluent from the chlorination reaction operation needs no separation, but the effluent from the pyrolysis operation is a mixture that needs to be separated into nearly pure species. Here, the source of the three species in the effluent is at a composition far different from the compositions of the three sinks: vinyl-chloride product, HCl byproduct, and the dichloroethane for recycle. To eliminate these composition differences, one or more separation operations are needed.

One possibility is shown in Figure 2.4, in which two distillation towers in series are inserted into the flowsheet. Distillation is possible because of the large volatility differences among the three species. This can be seen by examining

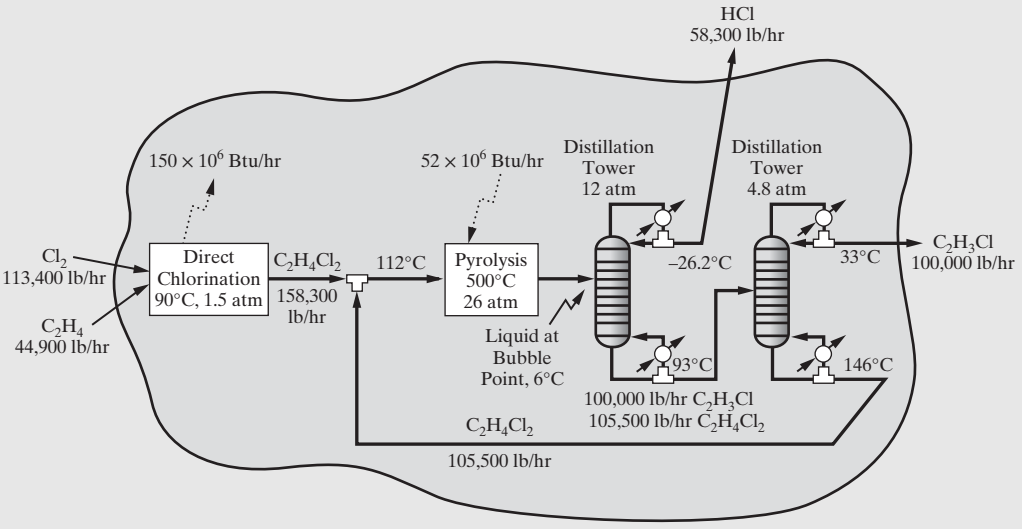


Figure 2.4 Flowsheet including the separation operations for the vinyl-chloride process.

Table 2.4 Boiling Points and Critical Constants

Chemical	Normal Boiling Point (1 atm, °C)	Boiling Point (°C) 4.8 atm	12 atm	26 atm	Critical Constants T_c(°C)	P_c(atm)
HCl	–84.8	–51.7	–26.2	0	51.4	82.1
C_2H_3Cl	−13.8	33.1	70.5	110	159	56
$C_2H_4Cl_2$	83.7	146	193	242	250	50

the boiling points in Table 2.4, which can be obtained from vapor pressure data in the preliminary database, or from a process simulator. In the first column, HCl is separated from the two organic chemicals. In the second column, vinyl chloride is separated from dichloroethane. At 1 atm, the boiling point of HCl is very low, −84.8°C, and hence if HCl were recovered at 1 atm as the distillate of the first tower, very costly refrigeration would be necessary to condense the reflux stream. At 26 atm (the pyrolysis reaction pressure), HCl boils at 0°C, and much less costly refrigeration could be used. The B.F. Goodrich patent recommends operation at 12 atm without any justification. At this pressure, HCl boils at –26.2°C and the bottoms product, comprised of vinyl chloride and dichloroethane with trace quantities of HCl, has a bubble point of 93°C, which can be calculated by a process simulator. The bottoms product at this reduced temperature and pressure is farther away from the critical points of vinyl chloride–dichloroethane mixtures at the bottom of the distillation column. It is likely, therefore, that B.F. Goodrich selected this lower pressure to avoid operation in the critical region where the vapor and liquid phases approach each other and are much more difficult to disengage (i.e., have small flooding velocities and require very large diameters and tray spacings). Furthermore, low-pressure steam is adequate for the reboiler. When this distillation tower is inserted into the flowsheet, the conditions of its feed stream, or sink, need to be identified. If the feed is a saturated liquid, the temperature is 6°C at 12 atm, with a mild refrigerant required for cooling. A preferable feed temperature would be 35°C or higher, which could be achieved by completing the cooling and partial condensation of the pyrolysis reactor effluent with cooling water, but the introduction of vapor into the column would increase the refrigeration load of the condenser at −26.2°C. Upon making this specification, key differences (temperature, pressure, and phase) appear between the effluent from the pyrolysis operation and the feed to the distillation column. These are eliminated in the next synthesis step by inserting temperature and pressure change operations, with each temperature specification leading to a somewhat different flowsheet.

After the first distillation operation is inserted into the flowsheet, the second follows naturally. The bottoms from the HCl-removal tower is separated into nearly pure species in the second tower, which is specified at 4.8 atm, as recommended by the B.F. Goodrich patent. Under these conditions, the distillate (nearly pure vinyl chloride) boils at 33°C and can be condensed with inexpensive cooling water, which is available at 25°C. The bottoms product boils at 146°C, and hence, the vapor boilup can be generated with medium-pressure steam, which is widely available in petrochemical complexes.

Note that bubble- and dew-point calculations, and phase equilibrium calculations, are discussed in Chapter 7; flooding velocities and the sizing of separation towers are discussed in Chapter 13. In summary, key decisions regarding the phases of streams (normally approximated at equilibrium) depend on the stream composition, temperature, and pressure. Iterative phase equilibrium calculations are needed to estimate bubble- and dew-point temperatures and pressures. These are normally carried out within the process simulators, even when positioning operations during process synthesis. But, in this textbook, the details of setting the stream conditions are discussed in Process Simulation Task-2 of Section 7.3 on process simulation.

Alternative separation operations can be inserted into Figure 2.3. When distillation is used, it is also possible to recover the least volatile species, dichloroethane, from the first column, and separate HCl from vinyl chloride in the second column. Yet another possibility is to use a single column with a side stream that is concentrated in the vinyl-chloride product. Absorption with water, at atmospheric pressure, can be used to remove HCl. The resulting vapor stream, containing vinyl chloride and dichloroethane, could be dried by adsorption and separated using distillation. With so many alternatives possible, the process designer needs time or help to select the most promising separation operations. As mentioned previously, this topic is considered in detail in Chapter 9.

Furthermore, as before, the synthesis tree in Figure 2.7 is augmented. In this case, the new branches represent the different flowsheets for the alternative separation operations. Clearly, as each step of the synthesis is completed, the tree represents many more possible flowsheets.

Step 4 Eliminate Differences in Temperature, Pressure, and Phase: When the reaction and separation operations are positioned, the states of their feed and product streams are selected. This is accomplished usually by adjusting the temperature and pressure levels to achieve the desired reaction conversions and separation factors. Subsequently, after the flowsheets have been created, these are often adjusted toward the economic optimum, often using the optimizers in the process simulators discussed in Chapter 21. In this synthesis step, however, the states are assumed to be fixed and operations are inserted to eliminate the temperature, pressure, and phase differences between the feed sources, the product sinks, and the reaction and separation operations.

Figure 2.5 shows one possible flowsheet. It can be seen that liquid dichloroethane from the recycle mixer at 112°C and 1.5 atm undergoes the following operations:

1. Its pressure is increased to 26 atm.
2. Its temperature is raised to the boiling point, which is 242°C at 26 atm.
3. Dichloroethane liquid is vaporized at 242°C.
4. Its temperature is raised to the pyrolysis temperature, 500°C.

Note that an alternative flowsheet would place operations 1 and 2 after operation 3. However, this is very uneconomical, as the cost of compressing a vapor is far greater than the cost of pumping a liquid because the molar volume of a vapor is so much greater than that of a liquid (typically, a factor

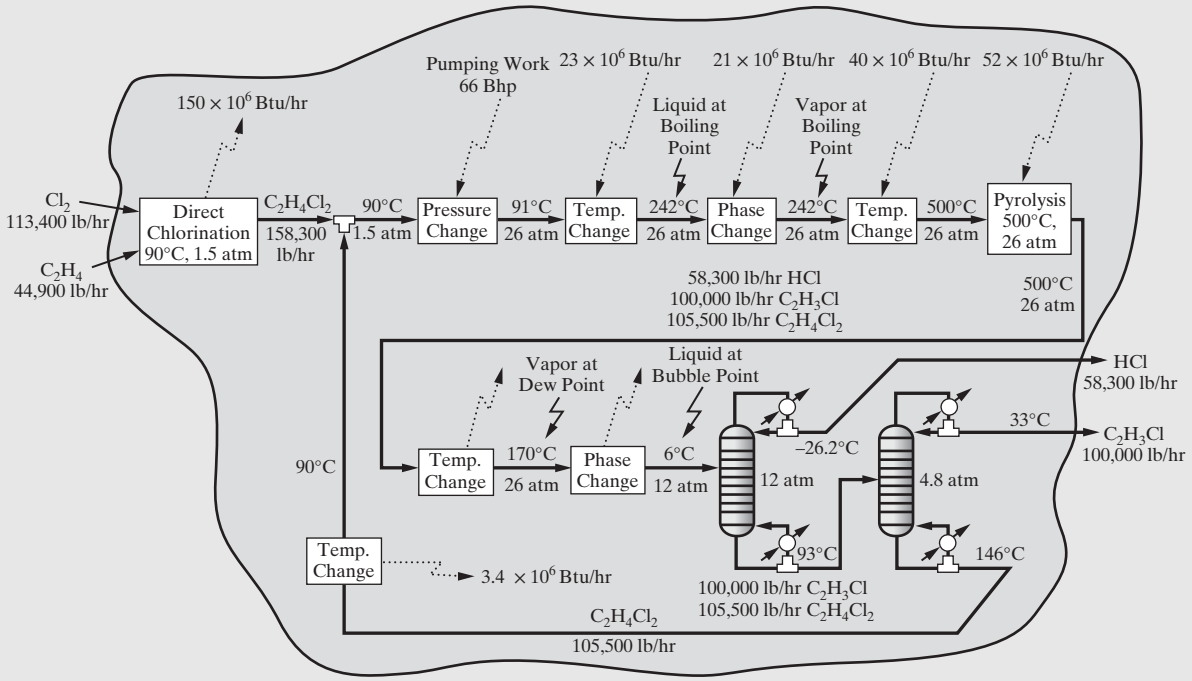


Figure 2.5 Flowsheet with temperature-, pressure-, and phase-change operations in the vinyl-chloride process.

of 100 times greater). For a more complete discussion of this observation, which is just one of many design heuristics or rules of thumb, see Section 6.7.

In addition, the hot vapor effluent from the pyrolysis operation (at 500°C and 26 atm) is operated upon as follows:

1. Its temperature is lowered to its dew point, 170°C at 26 atm.
2. The vapor mixture is condensed to a liquid at its bubble point, 6°C at 12 atm, by lowering the pressure and cooling and removing the latent heat of condensation.

Finally, the dichloroethane recycle stream is cooled to 90°C to avoid vaporization when mixed with the reactor effluent at 1.5 atm.

When positioning these operations, calculations to determine their heat duties and power loads are often carried out using process simulators. Methods for carrying out these energy balances are discussed in Process Simulation Task 3 of Section 7.3 on process simulators.

Branches to represent the two new flowsheets are added to the synthesis tree in Figure 2.7 after this synthesis step has been completed.

Step 5 Task Integration: At the completion of Step 4, each of the candidate flowsheets has a complete set of operations that eliminates the differences between the raw materials and the products. Still, with the exception of the distillation operations, specific equipment items are not shown. The selection of the processing units, often referred to as unit operations, in which one or more of the basic operations are carried out, is known as *task integration*. To assist in this selection, the reader is referred to *Chemical Process Equipment* (Walas, 1988).

Figure 2.6 shows one example of task integration for the vinyl-chloride process. At this stage in process synthesis, it is common to make the most obvious combinations of operations, leaving many possibilities to be considered when the flowsheet is sufficiently promising to undertake the preparation of a base-case design. As you examine this flowsheet, with the descriptions of the process units that follow, see if you can suggest improvements. This is one of the objectives in Exercise 2.3. Throughout the chapters that follow, techniques are introduced to obtain better integration for this and other processes that manufacture many other chemicals.

1. ***Chlorination reactor and condenser.*** The direct chlorination operation in Figure 2.5 is replaced by a cylindrical reaction vessel, containing a rectifying section, and a condenser. A pool of liquid dichloroethane, with ferric chloride catalyst dissolved, fills the bottom of the vessel at 90°C and 1.5 atm. Ethylene is obtained commonly from large cylindrical vessels, where it is stored as a gas at an elevated pressure and room temperature, typically 1,000 psia and 70°F. Chlorine, which is stored commonly in the liquid phase, typically at 150 psia and 70°F, is evaporated carefully to remove the viscous liquid (taffy) that contaminates most chlorine produced by electrolysis. Chlorine and ethylene in the vapor phase bubble through the liquid and release the heat of reaction as dichloroethane is produced. This heat causes the dichloroethane to vaporize and rise up the rectifying section into the condenser, where it is condensed with cooling water. Note that heat is needed to drive the reboiler in the first distillation column at 93°C, but the heat of reaction cannot be used for this purpose unless the temperature levels are adjusted. How can this be accomplished?

   Most of the condensate is mixed with the effluent from the recycle cooler to be processed in the pyrolysis loop. However, a portion is refluxed to the rectifying section of the column, which has several trays, to recover any of the less volatile species (e.g., trichloroethane) that may have vaporized. These *heavies* accumulate at the bottom of the liquid pool and are removed periodically as impurities.

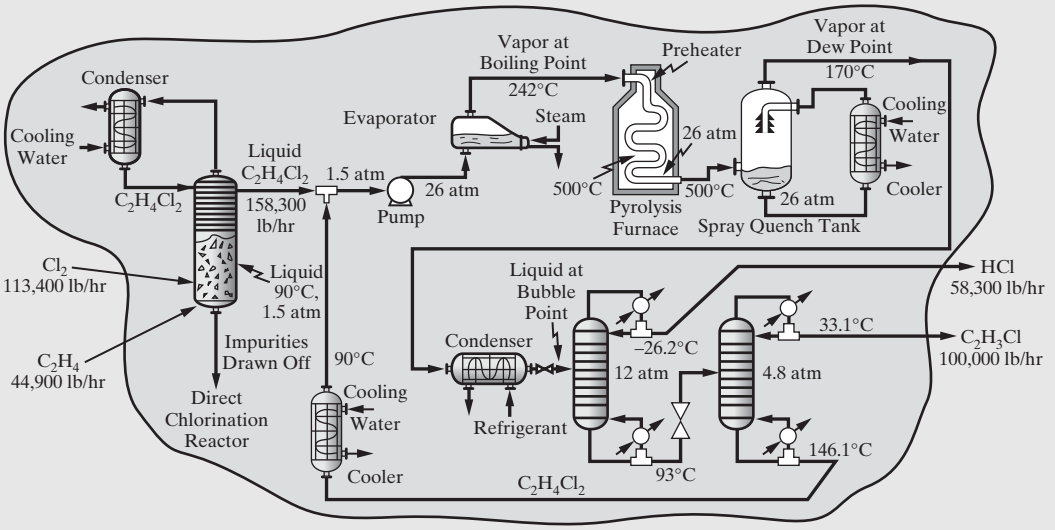


Figure 2.6 Flowsheet showing task integration for the vinyl-chloride process.

2. ***Pump.*** Since the pressure-change operation involves a liquid, it is accomplished by a pump, which requires only 66 Bhp, assuming an 80% efficiency. The enthalpy change in the pump is very small and the temperature does not change by more than 1°C.
3. ***Evaporator.*** This unit, in the form of a large kettle, with a tube bundle inserted across the bottom, performs the temperature- and phase-change operations. Saturated steam that passes through the tubes condenses as the dichloroethane liquid is heated to its boiling point and vaporized. The large vapor space is provided to enable liquid droplets, entrained in the vapor, to coalesce and drop back into the liquid pool, that is, to disengage from the vapor that proceeds to the pyrolysis furnace.
4. ***Pyrolysis furnace.*** This unit also performs two operations: It preheats the vapor to its reaction temperature, 500°C, and it carries out the pyrolysis reaction. The unit is constructed of refractory brick, with natural gas-fired heaters, and a large bundle of Nickel, Monel, or Inconel tubes, within which the reaction occurs. The tube bundle enters the coolest part of the furnace, the so-called *economizer* at the top, where the preheating occurs.
5. ***Spray quench tank and cooler.*** The quench tank is designed to rapidly quench the pyrolysis effluent to avoid carbon deposition in a heat exchanger. Cold liquid (principally dichloroethane) is showered over the hot gases, cooling them to their dew point, 170°C. As the gases cool, heat is transferred to the liquid and removed in the adjacent cooler. The warm liquid from the pool at the base of the quench vessel is circulated to the cooler, where it is contacted with cooling water. Any carbon that deposits in the quench vessel settles to the bottom and is bled off periodically. Unfortunately, this carbon deposition, as well as the corrosive HCl, is anticipated to prevent the use of the hot effluent gases in the tubes of the evaporator, which would have to be serviced often to remove carbon and replace corroded tubes. Note that coke formation in the pyrolysis products is discussed by Borsa et al. (2001). Consequently, large amounts of heat are transferred to cooling water, and the fuel requirements for the process are high. As noted later in the section on Checking the Key Assumptions in Process Synthesis, the design team is likely to measure the rate of carbon deposition and, if it is not very high, may decide to implement a design with a feed/product heat exchanger.
6. ***Condenser.*** To produce a saturated liquid at 6°C, the phase-change operation is carried out by a condenser that transfers heat to a mild refrigerant. Then the pressure is lowered to 12 atm across a valve.
7. ***Recycle cooler.*** To prevent vapor from entering the pump when the recycle stream is mixed with effluent from the direct chlorination reactor, the recycle stream is cooled to 90°C (below the boiling point of dichloroethane at 1.5 atm) using cooling water.

This completes the task integration in Figure 2.6. Can you suggest ways to reduce the need for fuel and hot utilities such as steam?

Synthesis Tree

Throughout the synthesis of the vinyl-chloride process, branches have been added to the synthesis tree in Figure 2.7 to represent the alternative flowsheets being considered. The bold branches trace the development of just one flowsheet as it evolves in Figures 2.1–2.6. Clearly, there are many alternative flowsheets, and the challenge in process synthesis is to find ways to eliminate whole sections of the tree without doing much analysis. By eliminating reaction paths 1 and 2, as much as 40% of the tree is eliminated in the first synthesis step. Similar screening techniques are applied by the design team in every step, as discussed throughout this book.

To satisfy the objective of generating the most promising flowsheets, care must be taken to include sufficient analysis in each synthesis step to check that each step does not lead to a less profitable flowsheet or exclude the most profitable flowsheet prematurely. For this reason, it is common practice in industry to mix these synthesis steps with analysis using the simulators introduced in Chapter 7.

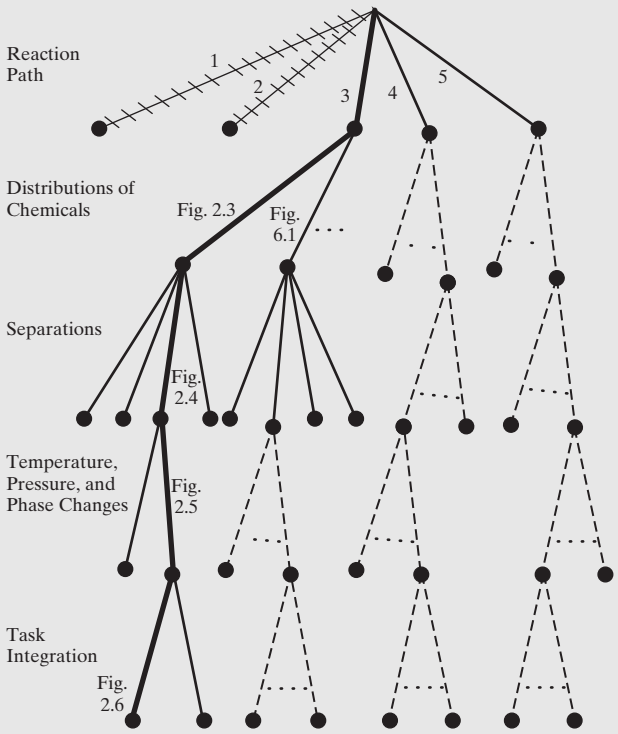


Figure 2.7 Inverted synthesis tree for the production of vinyl chloride. [Branch figure numbers must be 2.3, 2.4, 2.5, 2.6, 6.1.]

Heuristics

It is important to keep in mind that, when carrying out the steps in preliminary process synthesis, the resulting synthesis tree is closely related to any heuristics or rules of thumb used by the design team. In the vinyl-chloride example, emphasis was placed on the synthesis steps, not on the use of heuristics by the design team. An exception is the heuristic that it is cheaper to pump a liquid than compress a gas. Heuristics are covered more thoroughly in Chapter 6, where it will become clear that the synthesis tree can be improved significantly. See also *Conceptual Design of Chemical Processes* (Douglas, 1988) and Walas (1988), where many heuristics are presented.

Checking the Key Assumptions in Process Synthesis

After several promising flowsheets are synthesized, often the key assumptions are revisited before proceeding to the next steps in process design. Returning to Figure 2.6, one promising flowsheet for the vinyl-chloride process, a key limitation is that the cold $C_2H_4Cl_2$ stream is not heated by the pyrolysis products because the rate of carbon deposition in such a feed/product heat exchanger is anticipated to be high, and would cause the heat exchanger to foul with carbon. Instead, large quantities of heating utility (steam) are needed to vaporize the $C_2H_4Cl_2$ stream, and large quantities of cooling water utility are needed to cool the hot pyrolysis products. Before adopting this design, which uses excessive amounts of steam and cooling water, it becomes important to learn more about the rate of carbon deposition. Perhaps the rate is sufficiently low to allow the installation of a feed/product heat exchanger in which the carbon buildup is sufficiently low to require infrequent maintenance for carbon removal. Even at higher rates, to remove carbon deposits periodically, two heat exchangers could be installed in parallel, one of which would be operated while the other is being cleaned. This would provide substantial savings in steam and cooling-water utilities.

To check this and other assumptions, it is often desirable to construct a pilot plant that can produce quantities of product suitable for testing and evaluation by potential customers. Very few processes that include reaction steps are constructed without some form of pilot-plant testing prior to doing detailed design calculations. This is an expensive, time-consuming step that needs to be anticipated and planned for by the design team as early as possible, so as to avoid excessive delays. Also, for the vinyl-chloride process, kinetic data are needed for both the chlorination and pyrolysis reactors, as well as to determine the rate of carbon deposition. In all three cases, it is unlikely that adequate data can be located in the open literature. Consequently, unless sufficient data exist in company files or were taken in the laboratory and judged to be adequate, pilot-plant testing is needed. Generally, pilot-plant tests are conducted by a development team working closely with the design team.

Also, process simulators are often used during process synthesis, but Chapter 7 is entirely devoted to this subject.

Noncommodity Chemicals

For the manufacture of pharmaceuticals, specialty chemicals and materials, electronic materials, and foods, product throughputs are usually small leading to the design of batch, rather than continuous, processes. Example 2.3 discusses the process synthesis of such a batch process.

EXAMPLE 2.3 ***Manufacture of Tissue Plasminogen Activator (tPA)***

In the manufacture of pharmaceuticals, consider the possible production of plasminogen activators, which are powerful enzymes that trigger the proteolytic (breaking down of proteins to form simpler substances) degradation of blood clots that cause strokes and heart attacks. Since the mid-1980s, Genentech, a U.S. company, has manufactured tissue plasminogen activator (tPA), which they sold for $2,000 per 100-mg dose in the early 2000s, with annual sales of $300 MM/yr (MM in American engineering units is thousand-thousand, or 1 million). Given that their patent was set to expire in 2003, Genentech developed a next-generation, Food and Drug Administration (FDA)-approved, plasminogen activator called TNK-tPA, which is easier and safer for clinicians to use. With a rapidly growing market, the question arose as to whether an opportunity existed for another company to manufacture a generic (i.e., without a brand name) form of tPA that could compete favorably with TNK-tPA.

To examine this possibility, a design team was formulated.

It identified two potential alternatives:

Alternative 1. While a generic form of tPA may not compete well against TNK-tPA in the United States, it may be possible to market a low-cost generic tPA in foreign markets, where urokinase and streptokinase are low-cost alternatives, which sell for only $200/dose, but are associated with increased bleeding risks. Market analysis suggests that a maximum production rate of 80 kg/yr would be appropriate over the next five years.

Alternative 2. Given the possibility that lower health care reimbursements are received by hospitals in the United States, it may be reasonable to develop a similar process that competes favorably with TNK-tPA in the United States.

Other promising alternatives were likely to arise, often initiated by successes in a research laboratory.

Tissue plasminogen activator (tPA) is a recombinant therapeutic protein comprised of 562 amino acids, as shown schematically in Figure 2.8. Note that tPA is produced using a recombinant cell, which results from a recombination of genes. To eliminate blood clots, tPA activates plasminogen to plasmin, an enzyme, which dissolves fibrin formations that hold blood clots in place. In this way, blood flow is reestablished once the clot blockage dissolves, an important effect for patients suffering from a heart attack (microcardial infarction) or stroke. This example shows the steps in synthesizing a process to address the challenges posed by the opportunity suggested in alternative 1: that is, to manufacture less expensive forms of tPA that can be sold for $200 per 100-mg dose. Note that it leads to a batch process involving many small process units that must be scheduled for the manufacture of tPA, rather than a large-scale continuous process as for the manufacture of vinyl chloride.

Stated differently, based upon extensive research in the biochemistry laboratory, the tPA gene was isolated from human melanoma cells, and the process synthesis problem in Figure 2.9 created. As shown, tPA is produced using mammalian [e.g., Chinese hamster ovary (CHO)] cells that have tPA-DNA as part of their genetic contents (genome). In an aerobic bioreaction operation, the tPA-CHO cells grow in a nutrient media, HyQ PF-CHO—Hyclone media, a blend of nutrients, salts (including $NaHCO_3$), amino acids, insulin, growth factors, and transferrin, specifically for growth of CHO cells. Other ingredients include sterilized water, air, and CO_2. In addition to tPA, endotoxins may be a contaminant of the product, which must be removed because they elicit a variety of inflammatory responses in animals. Other byproducts include cell debris, wastewater, and gas emissions, especially N_2 from air, unconsumed O_2 from air, and CO_2, which regulates the pH. An important source of data, in addition to that taken in the biochemistry laboratory, is a U.S. patent, filed by Genentech (Goeddel et al., 1988), which provides considerable qualitative and quantitative information. See also the design report by Audette et al. (2000).

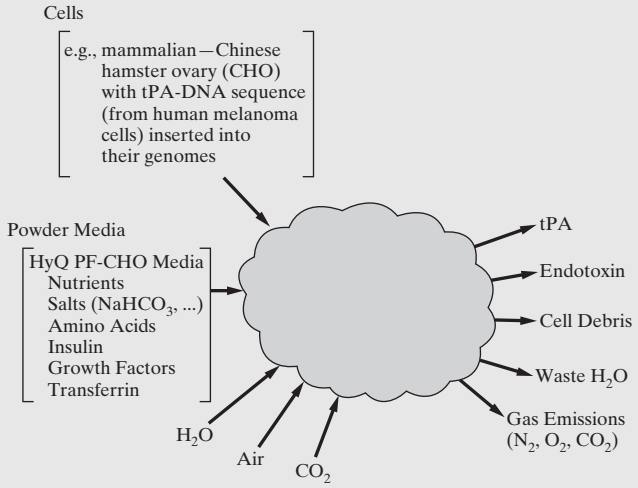


Figure 2.9 Process synthesis problem.

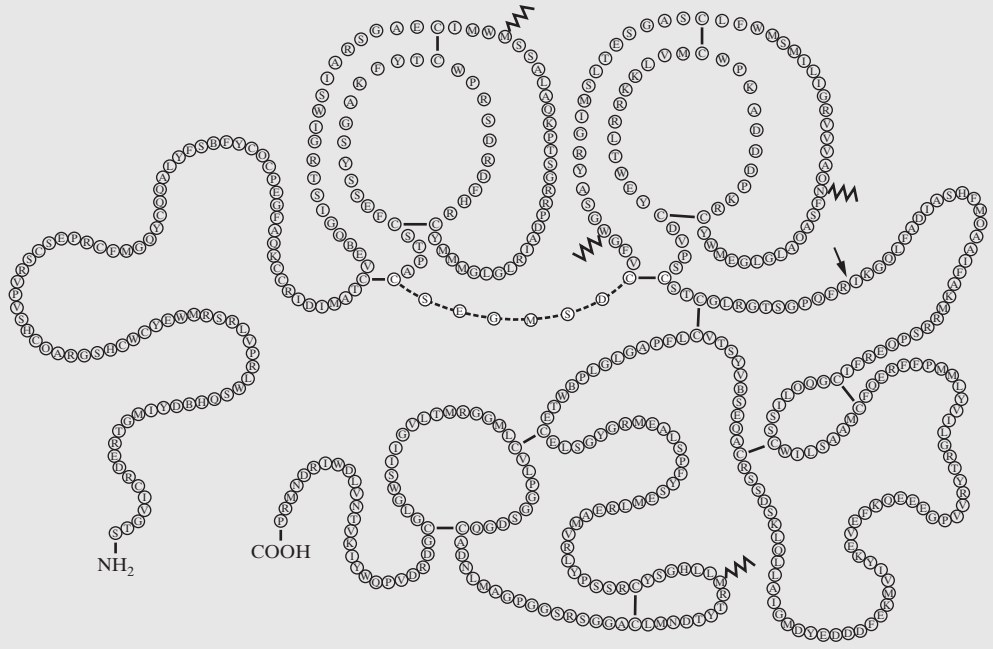


Figure 2.8 Schematic of tissue plasminogen activator (tPA).

Step 1 Eliminate Differences in Molecular Type: In the manufacture of a macromolecule like tPA through cell growth, a complex array of chemical reactions is often approximated by global reactions that are understood far less than the well-defined reactions for the manufacture of a simple monomer, like vinyl chloride. In terms of global reactions to manufacture tPA, two principal reaction paths are provided by the biochemist, as follows.

1. ***Mammalian Cells.*** Into CHO cells, the tPA-DNA sequence must be inserted and expressed. The resulting tPA-CHO cells are specially selected CHO cells with many copies of tPA-DNA inserted into their genomes, and which secrete high levels of tPA. This tPA-DNA insertion step is summarized in the reaction:

$$\begin{aligned}&\text{tPA} - \text{DNA sequence} + \text{CHO cells}\\ &\quad\rightarrow \text{selected high-expressing tPA}\\ &\quad\quad - \text{CHO cells}\end{aligned} \tag{2.8}$$

The product of this "catalyst preparation" is a master stock of tPA-CHO cells, which are prepared in the laboratory and stored in 1-mL aliquots at –70°C to be used as inoculum for the bioreaction:

$$\begin{aligned}&\text{tPA} - \text{CHO cells} + \text{HyQPF} - \text{CHO media}\\ &\quad + O_2 \rightarrow \text{Increased cell numbers}\end{aligned} \tag{2.9}$$

As the cells grow in this aerobic cultivation at a rate of 0.39×10^6 cell/(ml-day), oxygen from air is consumed at the rate of 0.2×10^{-12} mol O_2/(cell-hr), and tPA is produced at the rate of 50 picogram tPA/(cell-day). The latter is secreted gradually into the liquid media solution. Note that reaction (2.8) is carried out once during the research and development phase. Initially, 1–10 mg of tPA-DNA are added to 10^6 cells to produce a few tPA-CHO cells in many unmodified CHO cells. After careful selection, one tPA-CHO cell (the "founder" cell) is selected and amplified to yield about 2×10^6 cells/mL in 10–100 L. These cells are frozen in aliquots.

2. ***Bacterial Cells.*** A promising alternative is to insert the tPA-DNA sequence into the genome of *Escherichia coli (E. coli)* cells, as summarized by the reaction:

$$\begin{aligned}&\text{tPA} - \text{DNA sequence} + \textit{E.coli}\ \text{cells}\\ &\quad\rightarrow \text{selected high} - \text{expressing tPA}\\ &\quad\quad - \textit{E. coli}\ \text{cells}\end{aligned} \tag{2.10}$$

Then, the tPA-*E. coli* bacteria cells, which are grown in the laboratory, are frozen in aliquols at –70°C to be used as inoculum for the fermentation reaction:

$$\begin{aligned}&\text{tPA} - \textit{E. coli}\ \text{cells} + \text{powder media}\\ &\quad + O_2 \rightarrow \text{increased cell numbers}\end{aligned} \tag{2.11}$$

A batch fermentation of tPA–*E. coli* can produce 5–50 mg tPA/L-broth at harvest. *Escherichia coli* may require disruption to release tPA, which is then more difficult to separate. Should a process be synthesized based upon this reaction path, reaction rate data from the laboratory will be needed. Unlike CHO cells, *E. coli* cells do not add sugar groups (glycosylation) to tPA. Like CHO cells, tPA-*E. coli* cells are produced and frozen during the research and development phase.

Returning to the reaction path with CHO cells, using laboratory data, the reaction operation is inserted onto the flowsheet, as shown in Figure 2.10. At a production rate of 80 kg/yr of tPA, the lab reports that the following ingredients are consumed and waste products are produced:

Ingredients	kg/yr	Wastes	kg/yr
tPA-CHO cells	Small	Endotoxin	0.155
HyQ PF-CHO media	22,975	Cell debris	22,895
Water	178,250	Wastewater	178,250
Air	1,604	Gas emissions (N_2, O_2, CO_2)	4,036
CO_2	296		

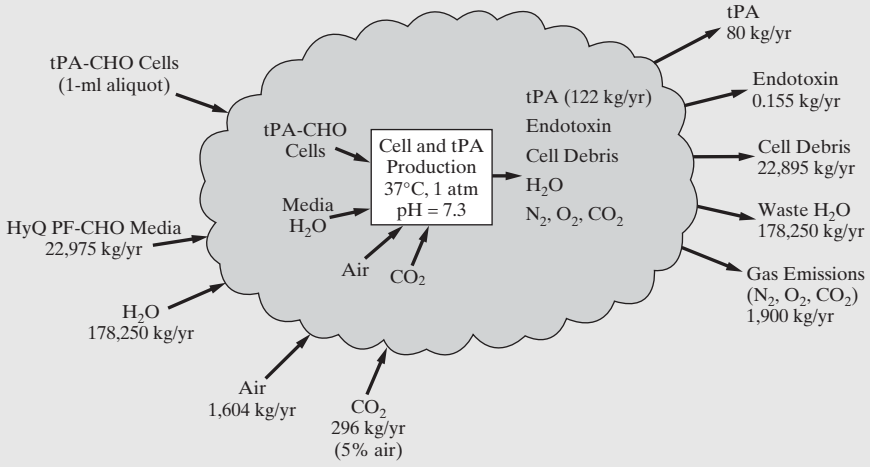


Figure 2.10 Reaction operations using mammalian CHO cells.

Table 2.5 Assumed Cost of Chemicals Produced or Sold

Chemical	kg/kg tPA	Cost ($/kg)
tPA	1	2,000,000
HyQ PF-CHO powder media	287.2	233
Water for injection (WFI)	2,228	0.12
Air	20.1	1,742
CO_2	3.7	1,447
tPA-CHO cells	—	a

[a]Not included in economic potential estimate—related to cost of research, an operating cost.

The reaction operation provides sinks for tPA-CHO cells from cold storage at –70°C, and HyQ PF-CHO media in water, air, and carbon dioxide. Its effluent is a source of tPA, at 122 kg/yr, endotoxin, cell debris, water, nitrogen, and carbon dioxide. When separated, these species are the sources for the product sinks from the flowsheet. Note that the combined cell growth and tPA production operation takes place at 37°C, 1 atm, and pH = 7.3. The latter is achieved by the $NaHCO_3$ in the powder media, with fine-tuning by manipulation of the flow rate of CO_2.

Before accepting a potential reaction path, it is important to examine the economic potential, that is, the difference between the sales revenues and the cost of ingredients. To accomplish this, the sales price of tPA is projected (e.g., $200 per 100-mg dose), and the costs of ingredients are projected, with estimates often obtained from the suppliers. A typical list of cost estimates is shown in Table 2.5. The cost of water for injection (WFI) is based upon estimates of the cost of sterilizing municipal water (12 cents/kg = 45 cents/gal = 450/1,000 gal, which is far higher than the typical cost of process water = $0.80/1,000 gal). The costs of sterilized air and carbon dioxide are for industrial cylinders of compressed gases. The cost of the tPA-CHO cells is not included, as it is associated with the cost of research, which is subsequently estimated as an operating cost.

Using these costs, the economic potential, *EP,* is estimated:

$$\begin{aligned} EP &= 2{,}000{,}000 - 287.2 \times 233 \\ &\quad - 2.228 \times 0.12 - 3.7 \times 1{,}447 \\ &\quad - 201.1 \times 1{,}742 \\ &= \$1{,}892{,}000/\text{kgtPA} \end{aligned}$$

Clearly, this is very high for tPA, a typical pharmaceutical. However, the economic potential does not account for the operating costs, which include the cost of research, the cost of utilities, and the investment cost, and are high for separations that involve expensive mass separating agents. With such a promising economic potential, the process synthesis proceeds at an accelerated pace.

Step 2 Distribute the Chemicals: In this step, the sources and sinks for each species in Figure 2.10 are matched so that the total mass flow rate into the reaction operation equals the mass flow rate out. This often entails the introduction of mixing operations, as illustrated in the previous example for vinyl chloride.

In this case, only one mixing operation is introduced, in which the HyQ PF-CHO powder media is mixed with water, as shown in Figure 2.11. Otherwise, the sources and sinks are matched directly. However, the effluent from the cell growth, tPA production reactor must be separated before its species are matched with the product sinks.

Step 3 Eliminate Differences in Composition: For most distributions of chemicals, composition differences exist between streams to be separated and the sinks to which these species are sent. Clearly, in Figure 2.11, the effluent from the cell growth, tPA production reactor must be separated.

Many separation system possibilities exist, with one provided in Figure 2.12. Here, the reactor effluent is sent to a separator for recovery of the gas emissions from the liquid mixture, with the latter sent to a centrifuge to remove wet cell debris from the harvest media or clarified broth. Note that because proteins lose their activity at temperatures above ~0°C, the centrifuge, and all other separation operations, are operated at

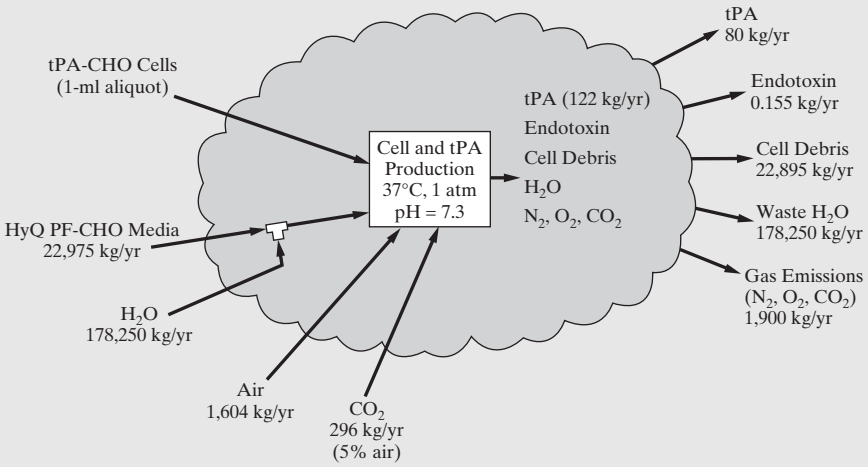


Figure 2.11 Flowsheet showing a distribution of chemicals for the tPA process.

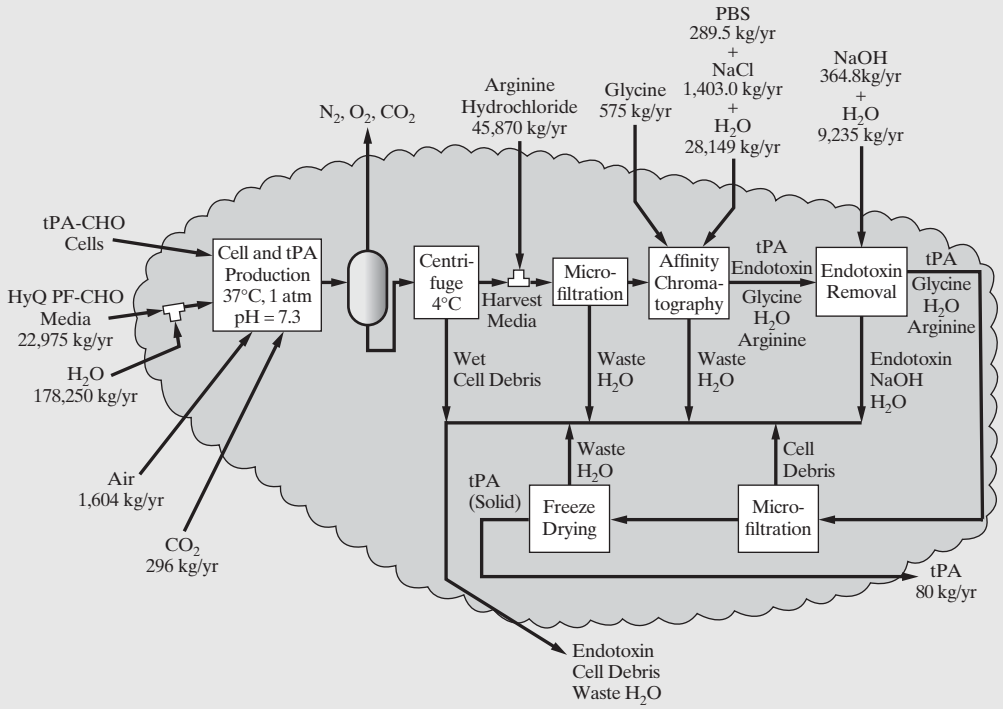
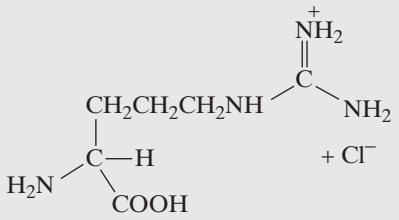


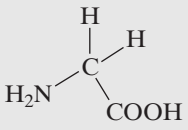
Figure 2.12 Flowsheet including the separation operations for the tPA process.

4°C, slightly above the freezing point of water. The harvest medium is mixed with arginine hydrochloride, an amino acid:



which prevents tPA from self-aggregating. Note that 45,870 kg/yr provides a concentration of 2.0 molar, which is sufficient to prevent aggregation.

The resulting mixture is sent to microfilters to remove large quantities of wastewater, which passes through the filters. For this step, alternate separators, like gel filtration and an Acticlean Etox resin (by Sterogene), should be considered. The retentate from the filter, which contains tPA, other proteins, endotoxin, arginine hydrochloride, and some water, is sent to an affinity chromatography operation. Here, tPA is selectively adsorbed on a resin (e.g., CNBr-activated Sepharose, by Amersham Biotech). The resin is then eluted with glycine, an amino acetic acid:



From lab measurements, 575 kg/yr of glycine are sufficient for the elution process. After the column is eluted, it is equilibrated with a mixture of 289.5 kg/yr of phosphate buffer solution (PBS) and 1,403.0 kg/yr of NaCl, with the quantities determined in the lab.

The resulting tPA solution is sent to an endotoxin removal column where the endotoxin is adsorbed selectively onto a resin (e.g., Acticlean Etox by Sterogene). This column is washed with a mixture of 364.8 kg/yr of NaOH and 9,235 kg/yr of water to remove the endotoxin. The effluent stream is microfiltered to remove cell debris that does not pass through the filter. Then, wastewater is removed in a freeze-drying operation to provide tPA in powder form.

Step 4 Eliminate Differences in Temperature, Pressure, and Phase: In the manufacture of tPA, the ingredients are assumed to be available at 20°C, water is mixed with the HyQ PF-CHO powder media at 4°C, the cultivations (cell production operations) occur at 37°C, and the separations occur at 4°C. The exothermic heat of the cultivation is removed at 37°C. Only small pressure changes occur and can be neglected at this stage of process synthesis. Similarly, no phase-change operations are added to the flowsheet. Hence, only a few temperature-change operations are added to Figure 2.12, with the resulting flowsheet shown in Figure 2.13.

Step 5 Task Integration: At this stage in the synthesis, various items of equipment are selected, often combining two or more adjacent operations into a single equipment item; that is, in task *integration*. The first key decision involves whether to operate in continuous or batch mode. For small throughputs, such as 80 kg/yr of tPA, the decision is nearly always to operate in batch mode. Choices of batch and equipment sizes, and batch time, are usually based upon the slowest operation, usually the cultivation (or fermentation) process. For tPA, it is determined using the experimental growth rate of tPA-CHO cells [0.39×10^6cell/(mL-day)], the inlet and outlet cell concentrations, and the experimental rate of tPA growth [50 pg tPA/(cell-day)], where pg ≡ picogram ≡ 10^{-12} g. One approach is shown next in Sub-Example 2.3.1.

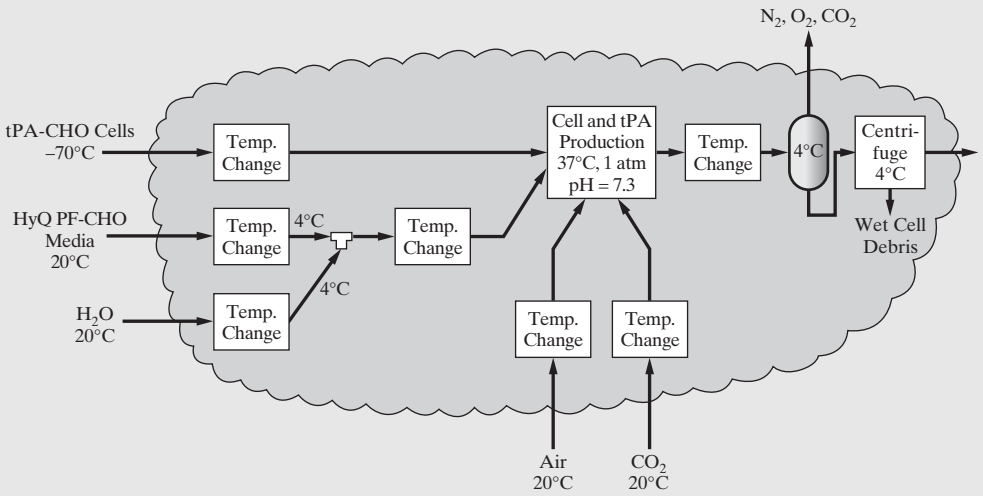


Figure 2.13 Flowsheet with the temperature-change operations in the tPA process.

SUB-EXAMPLE 2.3.1 Estimating Batch Time and Vessel Size

For nearly all cell cultivations, multiple cultivators are needed. As indicated in Step 1 of this process synthesis, 1 L of inoculum is grown in the laboratory, containing tPA-CHO cells at 2×10^6cell/mL. Next, cells are diluted and grown in progressively larger vessels. In each vessel, they are diluted to concentrations beyond which the experimental growth rate can be achieved for tPA-CHO cells, on the order of 10^5 cell/mL. Then, they are permitted to grow to concentrations limited by overcrowding, on the order of 3×10^6cell/mL for tPA-CHO cells.

As will be shown in this task integration, the last cultivator produces nearly all of the product tPA. Consequently, it is the basis for selection of batch and equipment sizes, and batch time. For typical limiting concentrations

$$c_{min} = 2 \times 10^5 \text{ cell/mL}$$
$$c_{max} = 3 \times 10^6 \text{ cell/mL}$$

the cultivation time is estimated:

$$\frac{3 \times 10^6 \frac{\text{cell}}{\text{mL}} - 2 \times 10^5 \frac{\text{cell}}{\text{mL}}}{0.39 \times 10^6 \frac{\text{cell}}{\text{mL-day}}} = 7.2 \text{ day} \cong 7 \text{ days}$$

Adding 7 days for loading, cleaning, and sterilizing the vessel, a total of 14 days are required.

Next, 50 batches annually are assumed. At two weeks per batch, two batch vessels operating in parallel are required; that is, two batch trains, each manufacturing 25 batches per year are needed. To produce 80 kg tPA/yr, the batch size is:

$$\frac{80 \text{ kg tPA}}{50 \text{ batch}} = 1.6 \frac{\text{kg tPA}}{\text{batch}}$$

One final assumption is needed. Early in the design, before the details of the separation train are considered, a 40% loss of tPA is assumed in the separations operations. Hence, $1.6 \times 1.4 = 2.24$ kg/batch must be produced in the cultivations.

Finally, at an average concentration of $(2 \times 10^5 + 3 \times 10^6)/2$ cell/mL $= 1.6 \times 10^6$cell/mL, the tPA growth per batch is

$$2{,}240 \frac{\text{g tPA}}{\text{batch}} = V \times 1.6 \times 10^6 \frac{\text{cell}}{\text{mL}} \times 50 \frac{\text{pg tPA}}{\text{cell-day}} \times \frac{1 \text{ g tPA}}{10^{12} \text{pg tPA}} \times 7 \text{ days}$$

where V is the batch volume in the third cultivator. Solving, $V = 4 \times 10^6$mL/batch $= 4{,}000$ L/batch. For this purpose, a conventional 5,000 L vessel is used.

The flowsheet in Figure 2.14a begins with a 1-L laboratory cultivator, into which a 1-mL aliquot of tPA-CHO cells, at concentration 2×10^6 cell/mL, is charged from cold storage at −70°C (after defrosting). To this, HyQ PF-CHO media, water, air, and CO_2 are added. Next, the batch time for this lab cultivator is computed in Sub-Example 2.3.2.

SUB-EXAMPLE 2.3.2 Inoculum Growth in Laboratory

After the 1-mL aliquot is defrosted and added to the 1-L cultivator, it is diluted to a concentration:

$$\frac{1 \text{ mL}}{1{,}000 \text{ mL}} \times \left(2 \times 10^6 \frac{\text{cell}}{\text{mL}}\right) = 2 \times 10^3 \frac{\text{cell}}{\text{mL}}$$

Then, the lab-cultivator batch time is:

$$\frac{2 \times 10^6 \frac{\text{cell}}{\text{mL}} - 2 \times 10^3 \frac{\text{cell}}{\text{mL}}}{0.39 \times 10^6 \frac{\text{cell}}{\text{mL-day}}} = 5.12 \text{ days} \cong 5 \text{ days}$$

and the tPA growth is:

$$0.25 \frac{\text{g tPA}}{\text{batch}} = 1{,}000 \text{ mL} \times 10^6 \frac{\text{cell}}{\text{mL}} \times 50 \frac{\text{pg tPA}}{\text{cell-day}} \times \frac{1 \text{ g tPA}}{10^{12} \text{pg tPA}} \times 5 \text{ days}$$

a small fraction of the tPA growth in the entire cultivation process. Note that to the 1-L flask, HyQ PF-CHO media is added, along with ultra-pure water, air, and CO_2, to produce 1.2 kg/batch of inoculum.

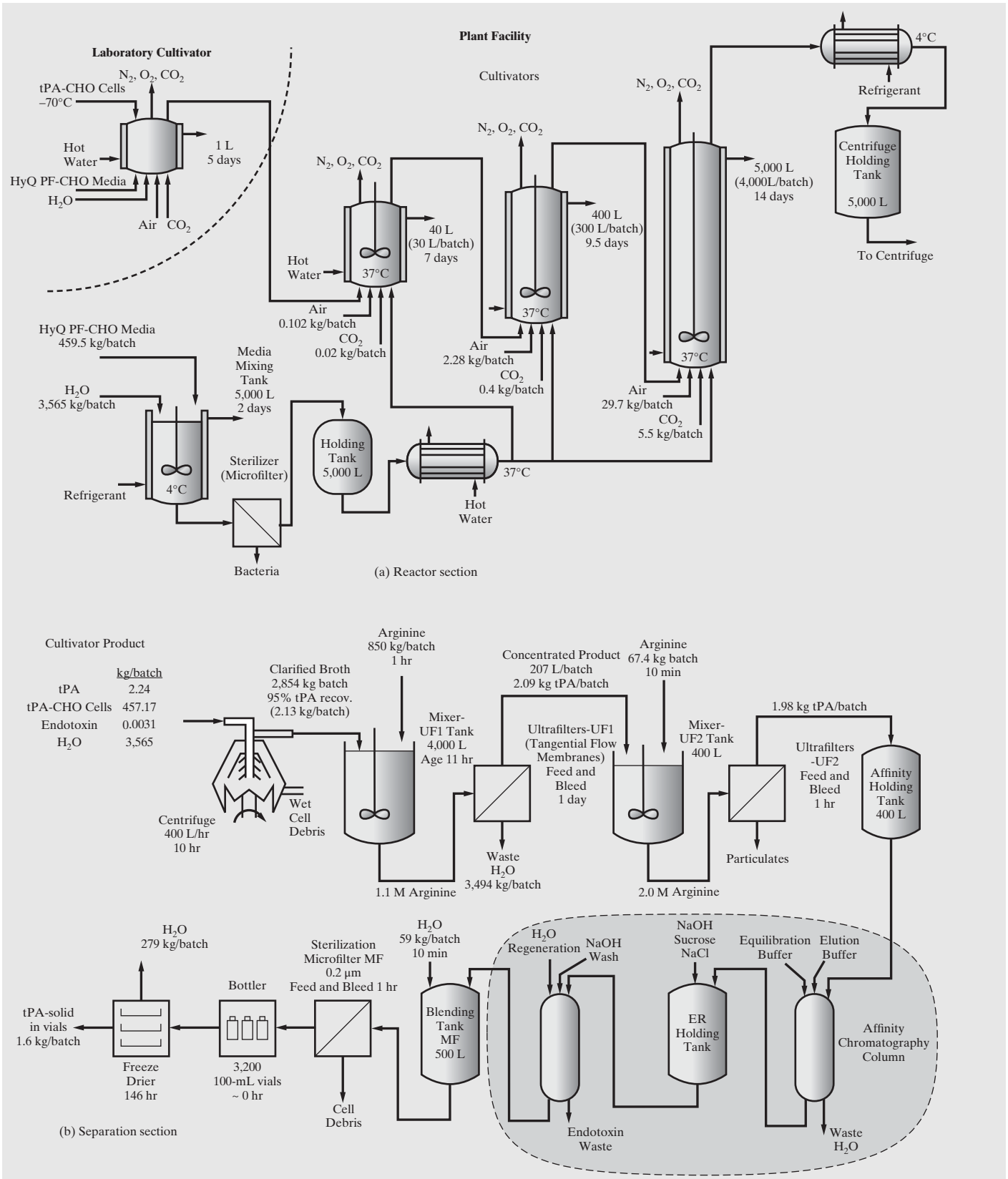
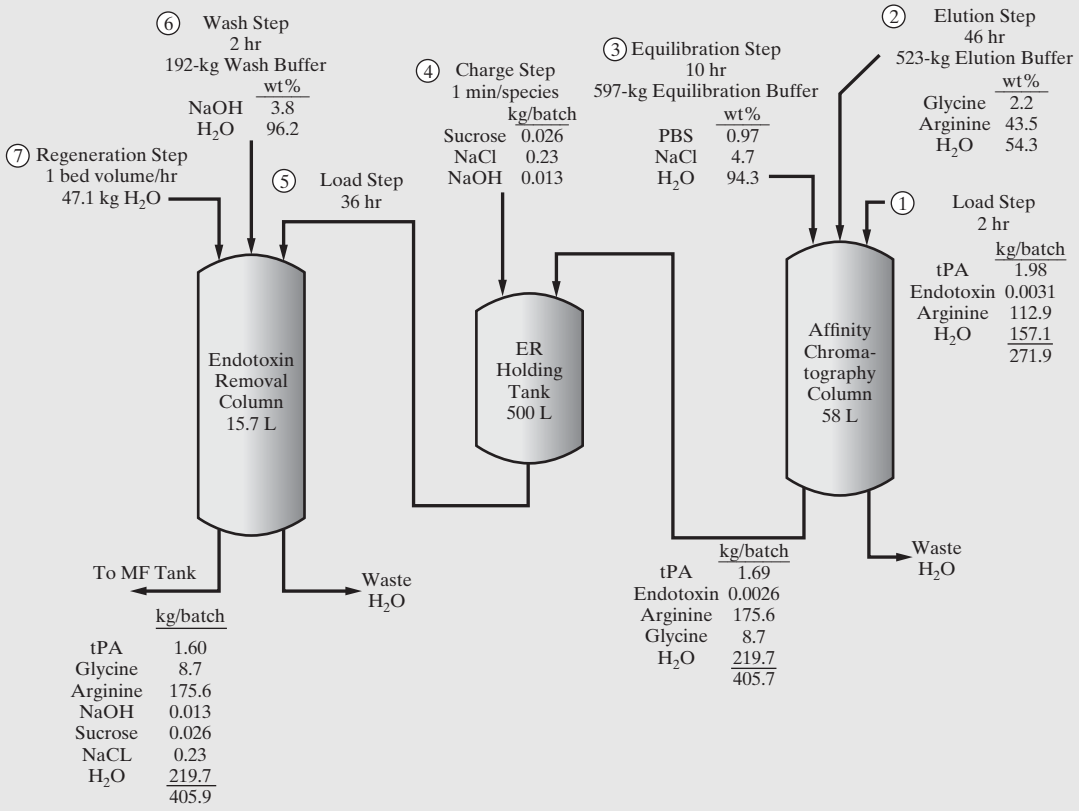


Figure 2.14 Flowsheet showing a task integration for the tPA process.



(c) Detailed separation section

Figure 2.14 (*continued*)

Next, the inoculum is taken to the plant, where it is added to the first of three cultivators, a 40-L cultivator selected to contain a 30-L batch after dilution. For this vessel, Sub-Example 2.3.3 shows how to compute the batch time, the tPA growth, and the air required.

SUB-EXAMPLE 2.3.3 Growth in Cultivator 1

After the inoculum is added to the 40-L cultivator, and diluted to 30 L, the cell concentration is:

$$\frac{1\text{ L}}{30\text{ L}} \times \left(2 \times 10^6 \frac{\text{cell}}{\text{mL}}\right) = 6.7 \times 10^4 \frac{\text{cell}}{\text{mL}}$$

Then, the growth time is:

$$\frac{2 \times 10^6 \frac{\text{cell}}{\text{mL}} - 6.7 \times 10^4 \frac{\text{cell}}{\text{mL}}}{0.39 \times 10^6 \frac{\text{cell}}{\text{mL-day}}} = 4.96 \text{ days} \cong 5 \text{ days}$$

Two days are added for loading, cleaning, and sterilization, to give a seven-day batch time.

At an average concentration of 1.03×10^6 cell/mL, the tPA growth is:

$$7.72 \frac{\text{g tPA}}{\text{batch}} = 30{,}000 \text{ mL} \times 1.03 \times 10^6 \frac{\text{cell}}{\text{mL}} \times 50 \frac{\text{pg tPA}}{\text{cell-day}} \times \frac{1 \text{ g tPA}}{10^{12} \text{ pg tPA}} \times 5 \text{ days}$$

and the O_2 consumed, at an experimental consumption rate of 0.2×10^{-12} mol O_2/cell-hr, is:

$$0.742 \frac{\text{mol O}_2}{\text{batch}} = 30{,}000 \text{ mL} \times 1.03 \times 10^6 \frac{\text{cell}}{\text{mL}} \times 0.2 \times 10^{-12} \frac{\text{mol O}_2}{\text{cell-hr}} \times \frac{24 \text{ hr}}{\text{day}} \times 5 \text{ days}$$

The weight fraction of O_2 in air is 0.233, which gives 0.102 kg air/batch.

Next, Sub-Example 2.3.4 provides similar calculations for the second and third cultivators in the plant, as shown in Figure 2.14a.

SUB-EXAMPLE 2.3.4 Growth in Cultivators 2 and 3

Cultivator 2

The second cultivator is 400 L, with contents diluted to 300 L, to give a cell concentration:

$$\frac{30\text{ L}}{300\text{ L}} \times \left(2 \times 10^6 \frac{\text{cell}}{\text{mL}}\right) = 0.2 \times 10^6 \frac{\text{cell}}{\text{mL}}$$

Its growth time is:

$$\frac{3 \times 10^6 \frac{\text{cell}}{\text{mL}} - 0.2 \times 10^6 \frac{\text{cell}}{\text{mL}}}{0.39 \times 10^6 \frac{\text{cell}}{\text{mL-day}}} = 7.2 \text{ days}$$

Here, 2.3 days are added for loading, cleaning, and sterilization, to give a 9.5-day batch time.

At an average concentration of 1.6×10^6 cell/mL, the tPA growth is:

$$173 \frac{\text{g tPA}}{\text{batch}} = 300{,}000 \text{ mL} \times 1.6 \times 10^6 \frac{\text{cell}}{\text{mL}} \times 50 \frac{\text{pg tPA}}{\text{cell-day}} \times \frac{1 \text{ g tPA}}{10^{12} \text{ pg tPA}} \times 7.2 \text{ days}$$

and the O_2 consumed, at an experimental consumption rate of 0.2×10^{-12} mol O_2/cell-hr, is:

$$16.6 \frac{\text{mol } O_2}{\text{batch}} = 300{,}000 \text{ mL} \times 1.6 \times 10^6 \frac{\text{cell}}{\text{mL}} \times 0.2 \times 10^{-12} \frac{\text{mol } O_2}{\text{cell-hr}} \times \frac{24 \text{ hr}}{\text{day}} \times 7.2 \text{ days}$$

The weight fraction of O_2 in air is 0.233, which gives 2.28 kg air/batch.

Cultivator 3

The third cultivator is 5,000 L, with contents diluted to 4,000 L, to give a cell concentration:

$$\frac{300 \text{ L}}{4{,}000 \text{ L}} \times \left(3 \times 10^6 \frac{\text{cell}}{\text{mL}}\right) = 0.225 \times 10^6 \frac{\text{cell}}{\text{mL}}$$

Its growth time is:

$$\frac{3 \times 10^6 \frac{\text{cell}}{\text{mL}} - 0.225 \times 10^6 \frac{\text{cell}}{\text{mL}}}{0.39 \times 10^6 \frac{\text{cell}}{\text{mL-day}}} \cong 7 \text{ day}$$

Here, 7 days are added for loading, cleaning, and sterilization, to give a 14-day batch time.

At an average concentration of 1.61×10^6 cell/mL, the tPA growth is:

$$2{,}254 \frac{\text{g tPA}}{\text{batch}} = 4{,}000{,}000 \text{ mL} \times 1.61 \times 10^6 \frac{\text{cell}}{\text{mL}} \times 50 \frac{\text{pg tPA}}{\text{cell-day}} \times \frac{1 \text{ g tPA}}{10^{12} \text{ pg tPA}} \times 7 \text{ days}$$

and the O_2 consumed, at an experimental consumption rate of 0.2×10^{-12}mol O_2/cell-hr, is:

$$216.4 \frac{\text{mol } O_2}{\text{batch}} = 4{,}000{,}000 \text{ mL} \times 1.61 \times 10^6 \frac{\text{cell}}{\text{mL}} \times 0.2 \times 10^{-12} \frac{\text{mol } O_2}{\text{cell-hr}} \times \frac{24 \text{ hr}}{\text{day}} \times 7 \text{ days}$$

The weight fraction of O_2 in air is 0.233, which gives 29.7 kg air/batch.

Adding the tPA growths in the laboratory and plant cultivators gives:

$$0.25 + 7.72 + 173 + 2{,}254 = 2{,}435 \text{ kg tPA/batch},$$

that is,

$$2{,}435 \text{ kg/batch} \times 50 \text{ batch/yr} = 121.7 \text{ kg tPA/yr},$$

which exceeds the throughput requirement of 80 kg tPA/yr by 52%, and should be adequate to cover anticipated separations losses. Note that, within limits, the bounding cell concentrations and batch volumes can be adjusted, affecting the batch times and tPA production rates. These parameters can be adjusted to optimize an objective function, for example, a profitability measure.

Finally, the air required for cultivation in the plant cultivators is:

$$0.102 + 2.28 + 29.7 = 32.1 \text{ kg air/batch},$$

that is,

$$32.1 \text{ kg/batch} \times 50 \text{ batch/yr} = 1{,}604 \text{ kg air/yr}$$

Returning to Figure 2.14a, note that to complete the reaction section of the process, a separate vessel for removal of gas emissions, containing N_2, O_2, and CO_2, is not needed, as these are vented continuously from the cultivators. Also, a 5,000-L mixing tank is installed to load and mix the powder media and water in two days. Note the tank jacket through which refrigerant is circulated. This vessel is followed by a microfilter, which sterilizes the mixture by removing bacteria, and a hot water heat exchanger. One last vessel, a 5,000-L holding tank, is provided to hold the contents of one cultivator batch (2.44, 457.17, 0.0031, 3,565 kg/batch of tPA, tPA-CHO cells, endotoxin, and water, respectively), in the event the centrifuge is taken off-line for servicing. The effluent from the third cultivator is cooled to 4°C in the shell-and-tube heat exchanger, which is cooled by a refrigerant on the shell side.

Turn next to the separation section in Figure 2.14b. The centrifuge is designed to handle small batches, at a rate of 400 L/hr over 10 hr. It rotates at high speed with the wet cell mass (which contains all of the tPA-CHO cells, 5 wt% of the tPA, 20 wt% of the water, and none of the endotoxin fed to the centrifuge) thrown to the outside collection volume and removed. Note that at this stage in process synthesis, recovery fractions are estimated using heuristics and experimental data when available. Also, since the endotoxin contaminant must be removed entirely, it is assumed to be entirely recovered (100%) in the effluent from the microfilters. The clarified broth (2,854 kg/batch) exits through the central tube overhead. It enters a mixing tank in which arginine hydrochloride is added to form a 1.1 molar solution, which is microfiltered to remove 3,494 kg/batch of wastewater. The concentrated product, at 207 L/batch and containing 98, 5.62, and 5.62 wt% of the tPA, arginine hydrochloride, and water fed to the microfilter, is mixed with 67.4 kg/batch of arginine in a second mixing vessel to give 2.0 molar arginine. This solution is microfiltered lo remove particulate matter before being sent to the affinity holding tank. The effluent, which contains 95, 98, 100, and 98 wt% of the tPA, arginine, endotoxin, and water fed to the microfilter, is loaded into a 58-L affinity chromatography column, which adsorbs 100, 100, 2, and 2 wt% of tPA, endotoxin, arginine, and water, as shown in Figure 2.14c. Most of the adsorbed tPA, 1.69 kg/batch, is eluted with a stream containing glycine (523 kg/batch at 2.2, 43.5, and 54.3 wt% of glycine, arginine, and water, respectively) and sent to a 500-L holding tank (405.7 kg/batch containing 1.69, 8.7, 175.6, 0.0026, and 219.7 kg/batch of tPA, glycine, arginine, endotoxin, and water, respectively). Note that the edition buffer recovers 85 wt% of the tPA and endotoxin from the resin. The affinity chromatography column is equilibrated with an equilibration buffer (597 kg/batch containing 0.97, 4.7, and 94.3 wt% PBS, NaCl, and water, respectively). After a caustic and sucrose mix is added to the holding tank (0.013, 0.026, and 0.33 kg/batch of NaOH, sucrose, and NaCl, respectively), the mixture is loaded into the endotoxin removal column (406.0 kg/batch). In this 15.7-L column, the endotoxins are adsorbed, and removed, by washing with caustic (192 kg/batch containing 3.8 and 96.2 wt% NaOH and water, respectively), which is discarded. The endotoxin removal column is regenerated with 47.1 kg/batch of water, while the endotoxin-free solution (405.9 kg/batch containing 1.6, 8.7, 175.6, 0.013, 0.026, 0.23, and 219.7 kg/batch of tPA,

glycine, arginine, NaOH, sucrose, NaCl, and water, respectively) is sent to a holding tank, where 59 kg/batch of water are added. After sterilization with a microfilter to remove cell debris, from which 99.7% of the tPA is recovered, the solution is sent to a bottler and 100-mL vials, each containing 100 mg of tPA, are conveyed to a freeze-drier, where the water is evaporated.

It is important to recognize that the batch sizes in Figure 2.14 are representative. However, as discussed subsequently in Section 7.5 and Chapter 22, the batch times and vessel sizes are key design variables in scheduling and optimizing batch processes.

Synthesis Tree

Clearly, at each step in the synthesis of the process flowsheet, alternatives are generated and the synthesis tree fills in. For the tPA process, a schematic of a synthesis tree is shown in Figure 2.15. Note that the bold branch corresponds to the flowsheets in Figures 2.10–2.14. In design synthesis, the engineer strives to identify the most promising alternatives, eliminating the least promising alternatives by inspection, wherever possible. Initially, heuristic rules help to make selections. Eventually, algorithmic methods involving optimization can be introduced to check the heuristics and identify more promising alternatives, as discussed in Chapter 22. It should be emphasized, however, that the design window, beginning during Phases 1 and 2 of the clinical trials, is small, typically on the order of 12–16 months, before Phase 3 begins. Consequently, emphasis is normally placed on the rapid development of a promising design, and less on design optimization. Stated differently, for high-priced pharmaceuticals, it is far more important to be first to market rather than to achieve relatively small savings in the capital investment or operating expenses for the plant through design optimization. For further discussion, see Pisano (1997).

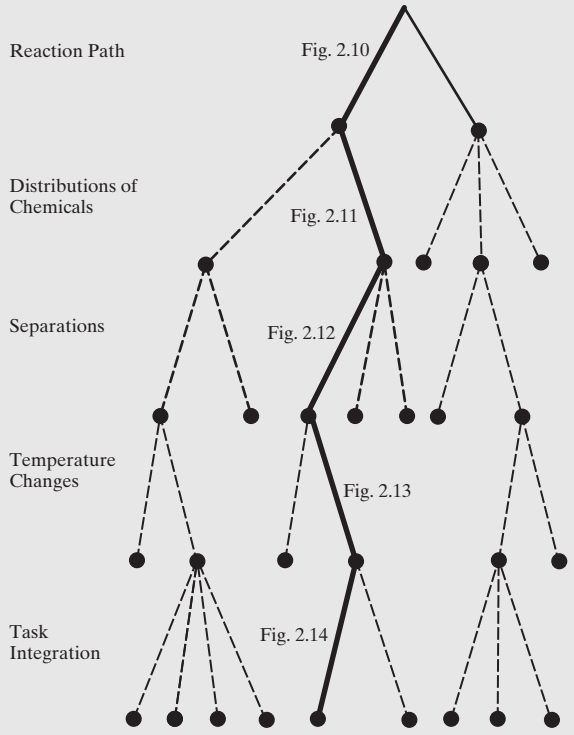


Figure 2.15 Inverted synthesis tree for the production of tPA.

2.4 NEXT PROCESS DESIGN TASKS

In the Introduction, Section 2.1, approaches for information gathering were discussed, given a process design problem statement. Then, in Section 2.2, the importance of experimentation when necessary was mentioned. These led to the key process design task, Preliminary Process Synthesis, which was discussed in Section 2.3 and illustrated to create alternative flowsheets for the manufacture of two chemical products, vinyl chloride and tissue plasminogen activator (tPA). In this section, Table 2.6 lists the remaining process design tasks, which are discussed briefly, beginning with Task-4, which involves a complete material balance for one of the promising process flowsheets—often referred to as the "base case" flowsheet. Also, for each task, the reader is referred to the chapter/section in this textbook in which approaches for carrying out the task are discussed.

Flowsheet Mass Balances

During preliminary process synthesis (Section 2.3), mass balances using approximate models are often carried out by using paper and pencil, spreadsheets, and even process simulators. For example, see Sub-Example 2.2.1. For a promising *base-case* flowsheet, block and initial process flow diagrams are often prepared, along with preliminary material balances, as shown in Section 2.5. Subsequently, mass balances are prepared using a process simulator as discussed in Chapter 7.

Process Stream Conditions

Also during preliminary process synthesis, initial stream conditions are specified, for example, temperatures and pressures, often at the bubble or dew points, or at specified vapor or liquid fractions. The latter are computed assuming phase equilibrium, often by a process simulator. In this textbook, the procedures for calculating phase equilibria and adjusting these specifications are discussed in Chapter 7 on the process simulators.

Flowsheet Material and Energy Balances

As shown earlier, simple energy balances are also carried out during preliminary process synthesis, often using a process simulator. Energy balances require estimates of the thermophysical properties (e.g., heat capacities, latent heats, internal energies, and enthalpies), which are commonly carried out by process simulators. Consequently, for base-case designs, strategies for carrying out material and energy balances for entire flowsheets are discussed in Chapter 7 on the process simulators. These are especially important for multicomponent recycle streams.

Equipment Sizing and Costing

Having completed material and energy balances for base-case designs, the next task normally involves estimating key equipment sizes and costs. Often these are estimated initially using approximate models by the process simulators as discussed in Chapter 7. Subsequently, more accurate models are inserted. For example, models to calculate the heat to be added or removed from a stream are replaced by models for shell-and-tube heat

Table 2.6 Process Design Tasks

Task	Description	Sources
1	Identify details about chemical product.	Section 2.1
2	Collect information about product's processing (e.g., raw materials, reaction paths).	Section 2.1
3	Carry out preliminary process synthesis. Select a promising base-case flowsheet.	Section 2.3, Chapters 6–11
4	Perform a mass balance on the flowsheet.	Section 2.5, Chapter 7
5	Decide on the process stream conditions.	Chapter 7
6	Perform material and energy balances on the flowsheet.	Chapter 7
7	Replace simple process unit models (e.g., heat requirement models), with more rigorous models (e.g., for a shell-and-tube heat exchanger).	Chapter 7
8	Perform equipment sizing and costing calculations for all equipment items.	Chapters 12–16, 27
9	Perform an economic evaluation for the process (e.g., a profitability analysis).	Chapter 17, 27
10	Seek opportunities for heat and mass integration.	Chapter 11, 27
11	Perform environmental impact and sustainability calculations. Check process safety.	Chapters 3
12	Check plantwide controllability.	Chapter 20
13	Seek to improve the design using process optimization.	Chapters 21, 22

exchangers. In this textbook, many of the details are provided in Chapters 12–16. Chapter 16 provides equations for estimating the sizes and costs of many equipment types.

Economic Evaluation

In some cases, just the total permanent investment is estimated, often approximately when comparing flowsheets during process synthesis. For promising base-case designs, more accurate calculations are carried out. In this textbook, Chapter 17 discusses in detail both the approximate and rigorous cost and profitability analysis methods.

Heat and Mass Integration

Often, as shown in Chapter 27 (Ammonia Process Design Case Study), heat and mass integrations are important to achieve profitable chemical processes. In this textbook, Chapter 11 thoroughly introduces the methods of heat integration, with the methods for mass integration introduced in a PDF file containing the supplement to Chapter 11.

Environment, Sustainability, and Safety

Throughout process synthesis and the subsequent tasks in process design, issues of environmental impact, sustainability, and process safety are considered carefully by most process design teams. In this textbook, Sections 3.3, 3.4, and 3.5, respectively, are devoted specifically to these issues. Also, many examples are discussed in the remaining chapters.

Controllability Assessment

It is important to check that the final flowsheet can be maintained at its desired operating conditions. There may be insufficient degrees of freedom to enable this to be carried out, and controllability assessment will uncover such deficiencies. In this textbook, Chapter 20 focuses on short-cut controllability assessment methods and introduces a conceptual plantwide control system configuration methodology, that will address these issues.

Optimization

Here, also, beginning with process synthesis, process design teams seek to select the best choices, often using optimizers within the process simulators. In this textbook, Chapter 21 focuses on optimization strategies often used in process design, with emphasis on steady-state operation of large-scale continuous processes. Chapter 22 covers the optimal design and scheduling of batch processes.

2.5 PRELIMINARY FLOWSHEET MASS BALANCES

As shown in Table 2.6, Task-4 in process design, which follows Task-3 (preliminary process synthesis), involves carrying out mass balances for the promising base-case process flowsheets. Having carried out some mass balances during process synthesis, this task is intended to complete the mass balance for the entire flowsheet, usually using approximate models and/or process simulators. Subsequently, more rigorous mass balances are carried out using process simulators (e.g., ASPEN PLUS, Aspen HYSYS, UniSim® Design, and PRO/II), as discussed in Chapter 7.

Because material balance results are normally displayed with process flow diagrams, this section discusses flow diagram conventions while presenting material balance results for the vinyl-chloride process synthesized in Example 2.2.

Flow Diagrams

Three kinds of flow diagrams are normally prepared to describe the base-case design(s). The first two, the *block flow diagram* and

the *process flow diagram*, are shown here for the vinyl-chloride process. The third, which includes the valves and process controllers, is the *piping and instrumentation diagram* (*P&ID*), which is especially important for control system design and safety (HAZOP) analysis, as discussed in Section 3.5.

Block Flow Diagram (BFD)

The block flow diagram represents the main processing sections in terms of functional blocks. As an example, Figure 2.16 shows a block flow diagram for the vinyl-chloride process, in which the three main sections in the process—namely, ethylene chlorination, pyrolysis, and separation—are shown, together with the principal flow topology. Note that the diagram also indicates the overall material balances and the conditions at each stage, where appropriate. This level of detail is helpful to summarize the principal processing sections and is appropriate in the early design stages, where alternative processes are usually under consideration.

Process Flow Diagram (PFD)

Process flow diagrams provide a more detailed view of the process. These diagrams display all of the major processing units in the process (including heat exchangers, pumps, and compressors), provide stream information, and include the main control loops that enable the process to be regulated under normal operating conditions. Often, preliminary PFDs are constructed using the process simulators. Subsequently, more detailed PFDs are prepared using software such as AUTOCAD and VISIO, the latter having been used to prepare Figure 2.17 for the vinyl-chloride process. The conventions typically used when preparing PFDs are illustrated using this figure and are described next.

Processing Units Icons that represent the units are linked by arcs (lines) that represent the process streams. The drawing conventions for the unit icons are taken from accepted standards, for example, the ASME (American Society for Mechanical Engineers) standards (ASME, 1961). A partial list of typical icons is presented in Figure 2.18. Note that each unit is labeled according to the convention U-XYY, where U is a single letter identifying the unit type (V for vessel, E for exchanger, R for reactor, T for tower, P for pump, C for compressor, etc.). X is a single digit identifying the process area where the unit is installed, and YY is a two-digit number identifying the unit itself. Thus, for example, E-100 is the identification code for the heat exchanger that condenses the overhead vapors from the chlorination reactor. Its identification code indicates that it is the 00 item installed in plant area 1.

Stream Information Directed arcs that represent the streams, with flow direction from left to right wherever possible, are numbered for reference. By convention, when streamlines cross, the

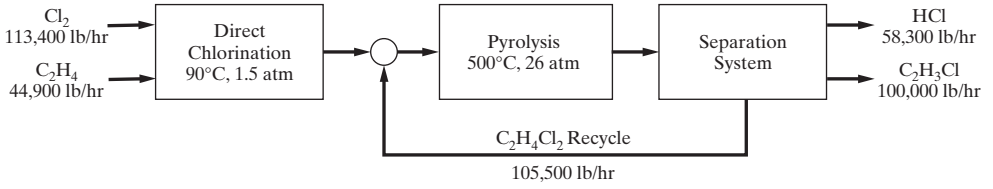


Figure 2.16 Block flow diagram for the vinyl-chloride process.

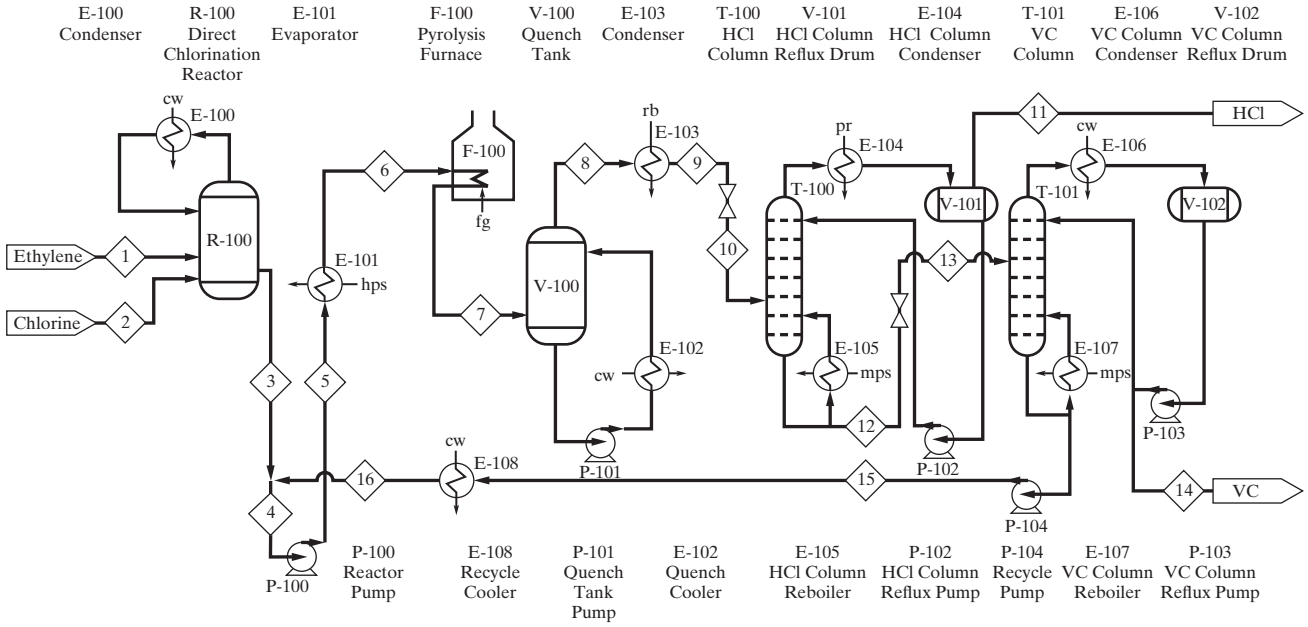


Figure 2.17 Process flow diagram for the vinyl-chloride process.

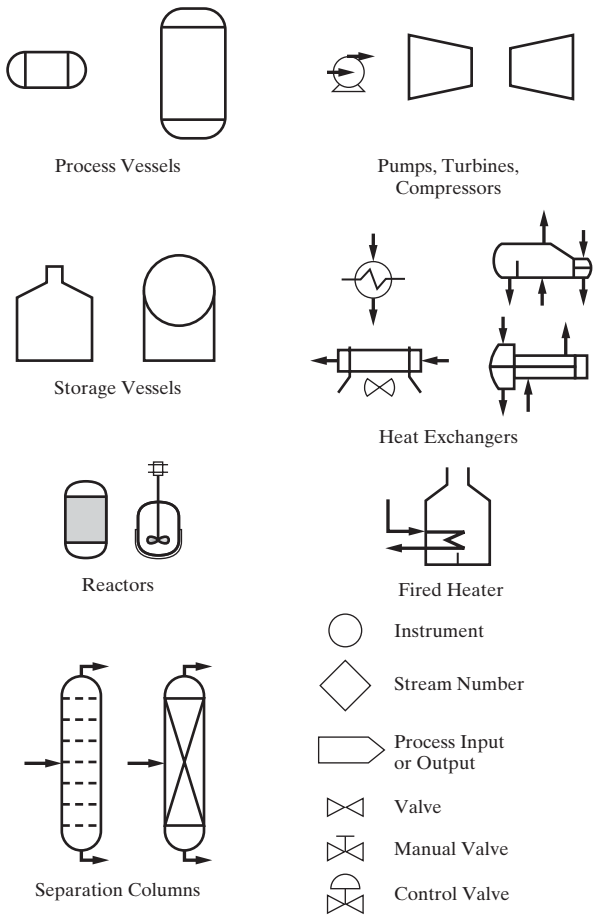


Figure 2.18 Icons in process flow diagrams.

horizontal line is shown as a continuous arc, with the vertical line broken. Each stream is labeled on the PFD by a numbered diamond. Furthermore, the feed and product streams are identified by name. Thus, streams 1 and 2 in Figure 2.17 are labeled as the ethylene and chlorine feed streams, respectively, while streams 11 and 14 are labeled as the hydrogen chloride and vinyl-chloride product streams, respectively. Mass flow rates, pressures, and temperatures may appear on the PFD directly, but more often are placed in the stream table instead, for clarity. The latter has a column for each stream and can appear at the bottom of the PFD or as a separate table. Here, because of formatting limitations in this text, the stream table for the vinyl-chloride process is presented separately in Table 2.7. At least the following entries are presented for each stream: label, temperature, pressure, vapor fraction, total and component molar flow rates, and total mass flow rate. In addition, stream properties such as the enthalpy, density, heat capacity, viscosity, and entropy may be displayed. Stream tables are often completed using a process simulator. In Table 2.7, the conversion in the direct chlorination reactor in assumed to be 100%, while that in the pyrolysis reactor in only 60%. Furthermore, both towers are assumed to carry out perfect separations, with the overhead and bottoms temperatures computed based on dew- and bubble-point temperatures, respectively.

Utilities As shown in Figure 2.17, various utility streams are utilized for heating or cooling the process streams. For example, E-100, the overhead condenser for the direct chlorination reactor, which operates at 90°C, is cooled using cooling water (*cw*). The other cooling utilities are refrigerated brine (*rb*) and propane

Table 2.7 Stream Summary Table for the Vinyl-Chloride Process in Figure 2.17

Stream Number	1	2	3	4	5	6	7	8
Temperature (°C)	25	25	90	90	91.3	242	500	170
Pressure (atm)	1.5	1.5	1.5	1.5	26	26	26	26
Vapor fraction	1.0	1.0	0.0	0.0	0.0	1.0	1.0	1.0
Mass flow (lb/hr)	44,900	113,400	158,300	263,800	263,800	263,800	263,800	263,800
Molar flow (lbmol/hr)	1,600	1,600	1,600	2,667	2,667	2,667	4,267	4,267
Component molar flow (lbmol/hr):								
Ethylene	1,600	0	0	0	0	0	0	0
Chlorine	0	1,600	0	0	0	0	0	0
1,2-dichloroethane	0	0	1,600	2,667	2,667	2,667	1,067	1,067
Vinyl chloride	0	0	0	0	0	0	1,600	1,600
Hydrogen chloride	0	0	0	0	0	0	1,600	1,600
Stream Number	9	10	11	12	13	14	15	16
Temperature (°C)	6	6.5	–26.4	94.6	57.7	32.2	145.6	90
Pressure (atm)	26	12	12	12	4.8	4.8	4.8	4.8
Vapor fraction	0.0	0.0	1.0	0.0	0.23	1.0	0.0	0.0
Mass flow (lb/hr)	263,800	263,800	58,300	205,500	205,500	100,000	105,500	105,500
Molar flow (lbmol/hr)	4,267	4,267	1,600	2,667	2,667	1,600	1,067	1,067
Component molar flow (lbmol/hr):								
Ethylene	0	0	0	0	0	0	0	0
Chlorine	0	0	0	0	0	0	0	0
1,2-dichloroethane	1,067	1,067	0	1,067	1,067	0	1,067	1,067
Vinyl chloride	1,600	1,600	0	1,600	1,600	1,600	0	0
Hydrogen chloride	1,600	1,600	1,600	0	0	0	0	0

Table 2.8 Heating and Cooling Utilities—Identifiers and Temperature Ranges

Identifier	Utility	Typical Operating Range
Hot Utilities—In increasing Cost per BTU:		
lps	Low-pressure steam, 15 to 30 psig	250 to 275°F
mps	Medium-pressure steam, 100 to 150 psig	325 to 366°F
hps	High-pressure steam, 400 to 600 psig	448 to 488°F
fo	Fuel oils	
fg	Fuel gas	Process waste stream
po	Petroleum oils	Below 600°F
dt	Dowtherms	Below 750°F
Cold Utilities—In increasing Cost per BTU:		
bfw	Boiler feed water	Used to raise process steam
ac	Air cooling	Supply at 85 to 95°F—temperature approach to process 4°F
rw	River water	Supply at 80 to 90°F (from cooling tower), return at 110°F
cw	Cooling water	Supply at 80 to 90°F (from cooling tower), return at 115 to 125°F
cw	Chilled water	45 to 90°F
rb	Refrigerated brine	0 to 50°F
pr	Propane refrigerant	–40 to 20°F

refrigerant (*pr*), each selected according to the temperature level of the required utility. Heating utilities are fuel gas (*fg*), high-pressure steam *(hps*), and medium-pressure steam (*mps*). A list of heating and cooling utilities, with temperature ranges, and the abbreviations commonly used on PFDs is presented in Table 2.8 (see also Table 17.1 and the subsection on *utilities* in Section 17.2).

Equipment Summary Table This provides information for each equipment item in the PFD, with the kind of information typically provided for each type of unit shown in Table 2.9. Note that the materials of construction (MOC), and operating temperature and pressure, are required for all units. Also note that suggestions for the materials of construction are provided in Appendix III.

In summary, the PFD is the most definitive process design document, encapsulating much of the commonly referred to design information. As such, it is used and updated throughout much of process design. However, it lacks many details required to begin the construction engineering work for the plant. Many of these details are transmitted in a *Piping and Instrumentation Diagram*.

Table 2.9 Equipment Summary Specifications

Equipment Type	Required Specification
Vessel	Height; diameter; orientation; pressure; temperature; materials of construction (MOC)
Towers	Height; diameter; orientation; pressure; temperature; number of and type of trays; height and type of packing; MOC
Pumps	Driver type; flow; suction and discharge pressures; temperature; shaft power; MOC
Compressors	Driver type; inlet flow; suction and discharge pressures; temperature; shaft power; MOC
Heat exchangers	Type; area; duty; number of shell and tube passes; for both shell and tubes: operating temperature; pressure; pressure drop; and MOC
Fired heaters	Type; tube pressure and temperature; duty; radiant; and convective heat transfer area; MOC

2.6 SUMMARY

Having studied this chapter, the reader should:

1. Be able to gather the data for use in the design of a manufacturing process, given a design problem statement.
2. Understand the five key steps in preliminary process synthesis and be able to use them to develop other flowsheets for the manufacture of vinyl chloride and tPA corresponding to the other branches of the synthesis trees in Figures 2.7 and 2.15, as well as the manufacture of other chemicals.
3. Be prepared to learn more about the 13 tasks in Table 2.6 normally carried out in preparing one or more base-case designs. Table 2.6 refers the readers to the sections and chapters that provide instructional materials.
4. After completing Task-3, Preliminary Process Synthesis, and creating promising base-case designs, be prepared to carry out Task-4 to create preliminary process flowsheets and mass balances.

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EXERCISES

2.1 For an equimolar solution of *n*-pentane and *n*-hexane, compute:

(a) The dew-point pressure at 120°F

(b) The bubble-point temperature at 1atm

(c) The vapor fraction, at 120°F and 0.9 atm, and the mole fractions of the vapor and liquid phases

2.2 Consider a stream at 400K containing 34 mol% *n*-pentane and 66 mol% *n*-hexane.

(a) What is the bubble point pressure?

(b) What are the mole fractions in the vapor at this pressure?

2.3 For the manufacture of vinyl chloride, assemble a preliminary database. This should include thermophysical property data, MSDSs for each chemical giving toxicity and flammability data, and the current prices of the chemicals.

2.4 For the vinyl-chloride process, using heats of formation, heat capacities, and latent heats, carry-out energy balances to determine the heats liberated and absorbed in the two reaction operations. Those computed using ASPEN PLUS, as shown in Figure 2.3, are:

(a) Direct chlorination = 150 million Btu/hr; note the reactants are at 25°C and the effluent stream is at 90°C; the pressure is 1.5 atm.

(b) Pyrolysis = 52 million Btu/hr; the reactant is at 90°C and the effluent stream is at 500°C; assume the pressure is 1 atm.

2.5 Consider the flowsheet for the manufacture of vinyl chloride in Figure 2.6.

(a) If the pyrolysis furnace and distillation towers are operated at low pressure (1.5 atm), what are the principal disadvantages? What alternative means of separation could be used?

(b) For the process shown, is it possible to use some of the heat of condensation from the $C_2H_4Cl_2$ to drive the reboiler of the first distillation tower? Explain your response. If not, what process change would make this possible?

(c) Consider the first reaction step to make dichloroethane. Show the distribution of chemicals when ethylene is 20% in excess of the stoichiometric amount and the chlorine is entirely converted. Assume that 100,000 lb/hr of vinyl chloride are produced.

(d) Consider the first distillation tower. What is the advantage of cooling the feed to its bubble point at 12 atm as compared with introducing the feed at its dew point?

(e) Why isn't the feed to the pyrolysis furnace heated with the hot pyrolysis products?

(f) What is the function of the trays in the direct chlorination 3 reactor?

(g) Suggest ways to reduce the need for fuel and hot utilities such as steam.

2.6 **(a)** To generate steam at 60 atm, two processes are proposed:

(1) Vaporize water at 1 atm and compress the steam at 60 atm.

(2) Pump water to 60 atm followed by vaporization.

Which process is preferred? Why?

(b) In a distillation tower, under what circumstances is it desirable to use a partial condenser?

2.7 Synthesize a flowsheet for the manufacture of vinyl chloride that corresponds to one of the other branches in the synthesis tree in Figure 2.7. It should begin with reaction path 4 or 5.

2.8 Using the chemical engineering literature, complete the detailed database for the detailed design of the base-case process in Figure 2.17. When appropriate, indicate the kind of data needed from a pilot plant and how this data should be regressed.

2.9 Consider the tPA process reactor (cultivation) section in Figure 2.14 (a):

(a) For the third cultivator, change the reaction time to three days. To obtain a cell concentration of 3×10^6 cell/mL, estimate the liquid volume in the cultivator. What reactor volume would you recommend?

(b) For (a), estimate the kg/batch of air consumed in the third cultivator.

2.10 In 2000, when the tPA process in Example 2.3 was synthesized using Chinese hamster ovary cells, data could not be located for the second reaction path using E-coli bacterial cells. Search the literature, especially the patents, since then to locate experimental results that give the:

(a) cell growth rate [cell/(mL-day)]

(b) tPA production rate [g/cell-day)]

(c) oxygen consumption rate [mol/(cell-hr)]

To check the patent literature, see Section 1.3 (*Feasibility Study* subsection). Can you locate data for other reaction paths?