E DESIGN PROJECTS I

The problems in this appendix are typical of industrial design problems. They are grouped into sections corresponding to different sectors of the chemical and fuels industries. Most of these are variants on commercially practiced technologies, but many are novel processes that may not yet be commercialized.

The problem statements are intentionally short, and little information is given beyond one or two references. Most of the problems are referenced to U.S. patents that give process concepts, chemical paths, and yield data, as this is often the starting point for technical and economic analysis in industrial design. There is no copyright on U.S. patents, and all of the referenced patents are available in the online material at http://books.elsevier.com/companions. Patent references are not given for older "traditional" processes, as flowsheets and yields for these processes can be found in the encyclopedias listed in Chapter 8.

An effort has been made to include a range of problems reflecting the broad spectrum of industries in which chemical engineers are employed. It must be recognized, however, that reliable price data for bulk quantities of specialty compounds may be hard to obtain. Many of the problems are therefore based on products and feeds for which the prices are listed in *ICIS Chemical Pricing* or *Oil and Gas Journal*.

Biochemical processes, i.e., processes that use enzymes, cells, or micro-organisms to effect chemical transformation or separation, are now prevalent in almost every sector of the chemicals industry. In almost any industry, chemical engineers are faced with process design and evaluation of biological processes. It therefore did not make sense to form a separate category of "biological processes" or "biochemicals," as these processes are just alternative routes to making commodity chemicals, polymers, fuels, pharmaceuticals, etc. Fourteen of the 101 design problems in this appendix involve biochemical processing steps. The sectors that do not have at least one biological process are inorganic chemicals, gas processing, electrochemical processes, and devices and sensors.

Many of the problems ask for a comparison between two designs and thus require two plants to be designed and costed. Most of the pharmaceutical problems are multistep processes that also require several plants to be designed. In many cases, the production rate is not given and must be estimated from an analysis of the market.

These problems are intended to be representative of typical problems that a design engineer might face in industry. A shorter selection of more structured problems with more background information is given in the next E-1.

E.1. COMMODITY CHEMICALS AND POLYMERS

E.1.1. Acetic Acid

Acetic acid is made by carbonylation of methanol. U.S. 5,001,259 (to Hoechst Celanese) describes changes to the reaction medium that improve catalyst stability and productivity. U.S. 3,769,329 (to Monsanto) describes the conventional process. Is it economically attractive to implement the changes proposed by the Hoechst patent in a new world-scale plant?

E.1.2. Acrolein and Acrylic Acid

Acrolein and acrylic acid are both made by vapor phase oxidation of propylene. U.S. 6,281,384 (to E. I. du Pont Nemours and Atofina) describes a fluidized bed process, while U.S. 5,821,390 (to BASF) describes an isothermal reactor cooled by heat transfer to a molten salt. U.S. 6,858,754 and U.S. 6,781,017 (both to BASF) describe alternative processes based on a propane feed. Compare the economics of acrylic acid production from propane with production from propylene. Is the conclusion different if the process is stopped at acrolein?

E.1.3. Cellulose Acetate

Cellulose acetate is used in films, cigarette filters, and moldings. It is made by reacting cellulose with acetic anhydride. U.S. 5,608,050 (to Eastman) describes an acetylation process that improves the thermal stability of the polymer. U.S. 5,962,677 (to Daicel) describes a process for improving the processing properties of the polymer. Estimate the cost of production of the polymer by each route.

E.1.4. Chloroform and Methylene Chloride

Chloroform and methylene chloride can be made by chlorination of methyl chloride. U.S. 5,023,387 describes the chlorination process and gives yields. Estimate the cost of production of chloroform for a plant that produces 40,000 metric tons per year. Chloroform is mainly used for making chlorodifluoromethane, which is a precursor for PTFE. Methylene chloride is used as a solvent, but the market for this compound is stagnant because of environmental concerns. How does the cost of production of chloroform change if the plant produces no methylene chloride?

E.1.5. Dicyclopentadiene

Dicyclopentadiene (DCPD) is usually recovered as a high value product from the byproduct pyrolysis gasoline stream that is generated in steam cracking furnaces (see “Ethylene and Propylene by Steam Cracking”). U.S. 6,258,989 (to Phillips Petroleum) gives a typical pyrolysis gasoline composition and describes a suitable recovery process. Estimate the NPV at 12% interest rate of a plant to recover DCPD from an 800,000 metric ton per year steam naphtha cracker.

E.1.6. 2,6-Dimethylnaphthalene

2,6-dimethylnaphthalene (2,6-DMN) is used to make 2,6-naphthalenedicarboxylic acid, which can be used to give improved properties to polyester bottle resins. Dimethylnaphthalenes can be made by reaction of butadiene with orthoxylene, yielding principally 1,5-DMN, which can then be isomerized to 2,6-DMN as described in U.S. 6,072,098 (to Mitsubishi Gas Chemical Company). An alternative purification process is described in U.S. 6,737,558 (to ENICHEM). Naphthalenic compounds can also be recovered from the light cycle oil (a diesel-range product) produced in oil refinery catalytic cracking units. Light cycle oil typically contains roughly 2% naphthalene, 4% methyl naphthalenes, 6% dimethyl naphthalenes, and 4% trimethyl naphthalenes. The distribution of naphthalene isomers can be approximated as the equilibrium distribution at 900°F. Compare the cost of producing 2,6-DMN from orthoxylene with the cost of recovering it from light cycle oil. Consider using additional processes to enhance the 2,6-DMN yield.

E.1.7. Ethylene and Propylene by Steam Cracking

Steam cracking of ethane is the most widely used process for making ethylene. U.S. 6,578,378 (to Technip-Coflexip) gives a typical ethane cracker product composition and describes an improved separation process for ethylene recovery. U.S. 5,990,370 (to BP) gives yields for ethane, propane, and mixtures. U.S. 5,271,827 (to Stone & Webster) gives details of furnace design and yields for a naphtha feed. Several other separation schemes for ethylene and propylene recovery are described in the literature. Estimate the cost of production for a new steam cracking facility that produces 1 million metric tons per year of ethylene and 600,000 metric tons per year of propylene. What feedstock would you recommend?

E.1.8. Ethylene by Oxidative Dehydrogenation

U.S. 6,548,447 and U.S. 6,452,061 (both to Regents of the University of Minnesota) suggest an alternative process for producing olefins such as ethylene from the corresponding paraffin using different catalysts. How does the cost of ethylene produced by this process compare with the cost of ethylene produced by the conventional steam cracking route?

E.1.9. Ethylene from Ethanol

Ethanol is usually made most economically from ethylene, and not vice versa; however, recent high natural gas prices and interest in ethanol from crops as a renewable raw material have prompted interest in the reverse process. U.S. 4,134,926 (to Lummus) describes a process for converting ethanol to ethylene with high yield.

What is the cost of ethylene produced by this route based on a fermentation ethanol feed?

E.1.10. Lactic Acid by Fermentation

U.S. 6,475,759 (to Cargill, Inc.) describes fermentation of corn steep liquor to lactic acid, and U.S. 6,229,046 (also to Cargill, Inc.) describes recovery of lactic acid from the fermentation broth. What is the cost of production of lactic acid by this route?

E.1.11. Linear Alkyl Benzenes

Linear alkyl benzenes (LAB) are starting compounds for making linear alkyl benzene sulfonates, which are widely used biodegradable surfactants. U.S. 5,012,021 (to UOP) describes a process for making LAB and U.S. 5,196,574 and U.S. 5,344,997 (also to UOP) give yields for several catalysts. Estimate the cost of production of the LAB and determine which catalyst is the best.

E.1.12. 2,6-Naphthalenedicarboxylic Acid

2,6-Naphthalenedicarboxylic acid is a precursor to polyethylene naphthalate (PEN), which is used to improve the properties of polyester bottle resins (see also problem E.1.6). It can be made by the liquid phase oxidation of 2,6-dimethylnaphthalene as described in U.S. 6,114,575, assigned to BP Amoco. Estimate the cost of production for a plant that produces 250,000 metric tons per year (250 kMTA).

E.1.13. Nitrobenzene

Nitrobenzene is a precursor for aniline and is made by nitration of benzene. U.S. 4,772,757 (to Bayer) describes an improved process with recycle of the nitrating acid. Estimate the cost of production for a plant that produces 150,000 metric tons per year.

E.1.14. Polylactic Acid

Polylactic acid is a biodegradable polymer. It can be made from lactic acid, which can be produced by fermentation of glucose. Because it is biodegradable and can be manufactured from agricultural products, polylactic acid is potentially a renewable material. US 6,326,458 assigned to Cargill Inc. describes a process for making polylactic acid from lactic acid. Estimate the cost of production of the purified polymer.

E.1.15. Phenol–Cyclohexanone

U.S. 6,720,462 describes a new process for phenol with co-production of a ketone. In example 3b, they suggest very high yields of phenol and cyclohexanone byproduct. Estimate the production cost of phenol by this route for a grassroots world-scale plant.

E.1.16. Propylene

Propylene is usually produced as a byproduct of ethylene manufacture. An alternative process is catalytic dehydrogenation of propane, as described in U.S. 4,381,417 (to UOP). What is the cost of production of propylene by this route for a world-scale plant?

E.1.17. Propylene Glycol by Fermentation

Propylene glycol (1,2-propanediol) is a commodity chemical. U.S. 6,087,140 (to Wisconsin Alumni Research Foundation) describes a process for fermentation of sugars to propylene glycol using transformed microorganisms. Estimate the maximum price that could be charged for the microorganisms.

E.1.18. Propylene Oxide by Epoxidation

A novel route for making propylene oxide is by epoxidation of propylene using hydrogen peroxide. U.S. 6,103,915 (to Enichem) and U.S. 5,744,619 (to UOP) give yields for several catalysts. U.S. 5,252,758 describes a process for propylene oxide production. Estimate the cost of propylene oxide production and determine the best catalyst.

E.1.19. Phosgene

Phosgene is an important intermediate in the manufacture of polycarbonate and polyurethane. U.S. 6,500,984 (to General Electric) describes a process for phosgene using carbon and silicon carbide catalysts. U.S. 6,054,104 (to DuPont) describes a process using a silicon carbide catalyst. U.S. 4,231,959 (to Stauffer Chemical) describes a process with recycle of unconverted CO. Estimate the cost of production for a world-scale plant. Which catalyst or combination of catalysts would you recommend?

E.1.20. Pyridine

Pyridine is an important chemical intermediate. U.S. 4,866,179 (to Dairen Chemical) describes a process for forming pyridine from ammonia and a carbonyl compound and gives yields for several aldehydes, ketones, and mixtures. U.S. 4,073,787 (to ICI) describes a process based on butadiene, formaldehyde, and ammonia. Estimate the cost of production for a world-scale plant and determine which feed is most economical.

E.2. DEVICES AND SENSORS

E.2.1. Fuel Processor

A fuel processor is a miniature hydrogen plant that converts a hydrocarbon fuel into hydrogen for use in a fuel cell. U.S. 6,190,623 (to UOP) describes a fuel processor for converting methane. Estimate the volume of a fuel processor unit using this technology for a 3 kW fuel cell system. What would the manufactured cost per unit be at a scale of production of 100,000 units per year?

E.2.2. Portable Oxygen Generator

Patients who have difficulty breathing are often given air enriched in oxygen. When the patient is immobile, the gas mixture can be supplied from cylinders, but when the patient is mobile, this may not be practical, particularly if the patient is weak. An alternative is to supply oxygen or enriched air by means of a portable oxygen generation device. US 6,764,534 (to AirSep Corp.) describes such a device, based on pressure swing adsorption. Estimate the cost of manufacturing this device based on a production volume of 10,000 units per year.

E.3. ELECTRONICS AND ELECTROCHEMICAL PROCESSES

E.3.1. Argon Recovery from Silicon Furnace Off-Gas

Argon is used as an inert atmosphere in silicon crystallization. U.S. 5,706,674 describes two processes for recovering spent argon. Which process is cheaper? How does the cost of this recovered argon compare with the cost of purchased argon?

E.3.2. Chlor-Alkali Manufacture

Chlorine and sodium hydroxide are made by the electrolysis of brine using membrane cells. Conventional and improved membrane cell arrangements are described in U.S. 4,391,693, assigned to Dow Chemical. U.S. 4,470,889 (also to Dow) gives data on membrane materials and performance. What price of electricity is needed for it to be economical to produce chlorine from sea water (3.5 wt% NaCl)?

E.3.3. Potassium Permanganate

Potassium permanganate can be made from potassium hydroxide and manganese dioxide ore using an electrolytic process, as described in U.S. 5,660,712 (unassigned, but clearly owned by Carus Corp.). Estimate the cost of manufacturing potassium permanganate.

E.4. FOOD PROCESSING AND FORMULATED PRODUCTS

E.4.1. Aspartame

Aspartame (α-L-aspartyl-L-phenylalanine 1-methyl ester) is a sweetening agent that is roughly 200 times sweeter than sucrose. Routes for preparing this compound are described in U.S. 3,492,131, U.S. 4,440,677 (both to G. D. Searle & Co.), and U.S. 5,476,961 (to the NutraSweet Company). Determine which route gives the lowest cost of production.

E.4.2. Cocoa Processing

Cocoa mass can be separated into cocoa powder and cocoa butter by solvent extraction, as described in U.S. 6,610,343, assigned to Cargill Inc. Cocoa butter is used in various food applications, while cocoa solids provide the flavor for chocolate and chocolate-flavored foods. The patent also describes several typical recipes for chocolate. Estimate the cost of producing milk chocolate and semisweet chocolate using the recipes given.

E.4.3. Dicalcium Phosphate and Phosphoric Acid

Dicalcium phosphate is used as a supplement to animal food. Food-grade phosphoric acid is used as an antioxidant and acidulant, for example, giving a sharp taste to soft drinks. U.S. 3,988,420 (to Israel Chemicals Ltd.) describes a process for making both products from phosphate rock and hydrochloric or nitric acid. Determine which acid leads to the highest net present value for a plant that produces 5000 metric tons per year of food grade dicalcium phosphate.

E.4.4. Erythorbic Acid

Erythorbic acid (also known as isoascorbic acid) is a preservative. It can be made by fermentation of glucose using various microorganisms, as described in U.S. 3,052,609 assigned to Sankyo Co. Estimate the cost of production and determine which microorganism is preferred.

E.4.5. Folic Acid

Folic acid is a vitamin (sometimes called vitamin M or vitamin Bc) found naturally in mushrooms, spinach, and yeast. It is an important dietary supplement during pregnancy, as it reduces the likelihood of spina bifida. U.S. 5,968,788 (to Toray Industries) describes conditions for cultivating several strains of yeast or bacteria to increase their yield of folic acid, and gives yields for each species. Determine the optimum strain and recovery process to make a USP product and estimate the cost of production via this route.

E.4.6. Insect Repellant

Insect repellants based on geraniol are described in U.S. 5,521,165 (to International Flavors & Fragrances). Estimate the cost of production of an aerosol-dispensed slow-release insect repellant formulation for spraying on skin and clothing.

E.4.7. Low-Fat Snacks

The difficulties of making fried snacks using nondigestible fats are described in U.S. 6,436,459 (to Procter & Gamble), which also gives recipes and compositions for potato-based low-fat snacks. Estimate the cost of producing low-fat snacks of the composition and recipe given in Example 1, using continuous frying.

E.4.8. Mannitol

U.S. 6,649,754 (to Merck) describes a process for making mannitol by hydrogenation of a mixture of glucose and fructose. U.S. 3,632,656 (to Atlas Chemical) describes recovery of mannitol from a mixture with sorbitol by crystallization from aqueous solution. U.S. 4,456,774 (to Union Carbide) describes an adsorptive separation of mannitol from sorbitol. U.S. 6,235,947 (to Takeda Chemical Industries) describes a process for recrystallizing mannitol to improve the crystal morphology and hence make a more compressible product that can be used in making tablets. Estimate the cost of production of Mannitol by the Merck route and determine which separation is most economical. What is the additional cost of making the recrystallized product via the Takeda route?

E.4.9. Margarine

The manufacture of margarine is described in U.S. 4,568,556 (to Procter & Gamble). Estimate the cost of making a stick margarine product of the recipe given in Example II. What is the NPV for a plant that produces 100,000 metric tons per year of margarine?

E.4.10. Moisturizing Lotion

U.S. 5,387,417 describes the formulation of a moisturizing lotion and the preparation of the emulsifying agent. Estimate the cost of production of each of the lotion formulations given in the patent.

E.4.11. Monosodium Glutamate

Monosodium glutamate (MSG) is a flavor enhancer. U.S. 2,877,160 (to Pfizer) and U.S. 2,978,384 (to Koichi Yamada) describe fermentation processes for glutamic acid. U.S. 5,907,059 (to Amylum Belgium & A. E. Staley Manufacturing) describes recovery of the fermentation product and conversion to MSG. Estimate the cost of production via this route.

E.4.12. Niacinamide (Nicotinamide)

Nicotinamide is a vitamin, also known as niacin and vitamin B_3. U.S. 4,681,946 (to BASF) describes a process based on amidation of nicotinic acid. U.S. 4,008,241 and U.S. 4,327,219 (both to Lummus) describe a process based on hydrolysis of nicatinonitrile. Which process has the lowest cost of production?

E.4.13. Riboflavin

Riboflavin (vitamin B2) can be made by fermentation, as described in U.S. 2,876,169 (to Grain Processing Corp.). The fermentation process has undergone many improvements. Newer strains with higher yields are described in U.S. 5,164,303 (to ZeaGen Inc.) and U.S. 4,794,081 (to Daicel Chemical). Alternative chemical routes are described in U.S. 2,807,611 (to Merck) and U.S. 4,687,847 (to BASF). Estimate the cost of producing a USP product via both the chemical and biochemical routes. Which process do you recommend?

E.4.14. α-Tocopherol

α-Tocopherol is the most bioactive form of vitamin E. It can be made by condensation of trimethylhydroquinone with isophytol, as described in U.S. 5,900,494 (to Roche Vitamins) or U.S. 7,153,984 (to DSM B.V.). Determine which process gives the lowest total cost of production.

E.5. FUELS

E.5.1. Benzene Reduction

Gasoline is usually produced as a blend of several petroleum streams that boil in the range of naphtha. A typical gasoline might contain 50% by volume of cracked naphtha with benzene content between 0.5 wt% and 2.0 wt% and 25% by volume of catalytically reformed naphtha with benzene content between 1 wt% and 3 wt%. Estimate the cost per gallon of gasoline of reducing the final benzene content to 0.62% by volume. Compositions of other components in the naphtha streams can be found in the patent literature.

E.5.2. Crude Oil Distillation

A typical crude oil distillation process was described in Chapter 4. Design a crude oil unit for a refinery that processes a 50:50 mixture (by volume) of Saudi Light and Saudi Heavy crude oils using the cut points given in Chapter 4.

E.5.3. Ethanol by Fermentation

Ethanol has a high octane value and is used as a gasoline blending component. It can be manufactured as a renewable fuel by fermentation of sugars using *S. cerevisae*. Compare the costs of producing ethanol from corn in Decatur, IL, and from sugar cane in Mobile, AL.

E.5.4. Hydrocracking

The hydrocracking process is used to crack heavy hydrocarbons to lighter hydrocarbons with addition of hydrogen. It is particularly useful for making distillate fuels such as jet fuel and diesel oil. U.S. 6,190,535 (to UOP) describes a novel hydrocracking process using a hot high-pressure stripping column, and gives an estimate of process yields. Estimate the NPV of a 40 kbd hydrocracker on the U.S. Gulf Coast using this technology.

E.5.5. Isomerization

The catalytic isomerization process is used to convert straight chain paraffin compounds in light naphtha into branched paraffins that have higher octane numbers and are more valuable as gasoline blending components. U.S. 6,008,427 (to UOP) describes the process flowsheet and U.S. 6,320,089 (also to UOP) gives yields for some new catalysts. Estimate the improvement in octane-barrel yield for the feed of Example VI in 6,320,089 using the process of 6,008,427. Estimate the NPV of a 10,000 bpd plant on a USGC basis at 12% interest rate. U.S. 6,472,578 (also to UOP) describes an improved separation scheme. What is the increase in NPV with this new scheme?

E.6. GAS PROCESSING

E.6.1. Gas to Liquids (Fischer-Tropsch Synthesis)

Conversion of natural gas to synthetic crude oil is a possible method for recovering stranded natural gas reserves. U.S. 4,624,968, U.S. 4,477,595, and U.S. 5,118,715 (all to Exxon Corp.) give yields for different catalysts. Determine the cost of producing a liquid product ($/bbl) if the natural gas is available at $0.50/1000 scf.

E.6.2. Hydrogen Production

Hydrogen is produced by steam reforming of natural gas. It is used as a raw material for ammonia and methanol production and for various applications in oil refining and chemicals production. Modern steam reforming plants use pressure swing adsorption to separate hydrogen from the other reaction products. The pressure swing adsorption plant can be integrated with the steam reforming section, as described in U.S. 4,869,894, assigned to Air Products. U.S. 4,985,231 (to ICI) describes a novel reforming reactor and gives examples of typical process yields. Estimate the cost (in $/Mscf) of supplying 100 MMscfd of hydrogen to an oil refinery on the U.S. Gulf Coast.

E.6.3. Krypton and Xenon Recovery

Krypton and Xenon are valuable gases present in very low concentrations in air. U.S. 6,662,593 assigned to Air Products describes a cryogenic distillation process for air separation with recovery of a stream concentrated in Kypton and Xenon. What would be the cost of producing purified Krypton and Xenon by this method? Consider reactive methods for separating Krypton and Xenon from the concentrated stream as well as the methods suggested in the patent.

E.6.4. Methanol to Olefins

Conversion of natural gas to liquids is currently of great interest, as many large natural gas fields are not close enough to large markets to make construction of a pipeline economically attractive. These "stranded" reserves can be liquefied, converted into fuels or converted into (higher value) petrochemicals. U.S. 5,714,662 (to UOP) describes a process for converting crude methanol to olefins. What is the cost of production of the ethylene produced by a plant that produces 900 kmta of mixed olefins if the cost of producing the natural gas feed is $0.5/MMbtu?

E.6.5. Natural Gas Liquefaction

U.S. 6,347,532 (Air Products) describes a process for liquefying natural gas and gives several possible process embodiments. Which of these is the cheapest for the given gas composition? If the gas initially contains 3000 ppmw CO_2, 1250 ppmw H_2S, and 28 ppmw COS, and the cost of producing the natural gas feed is $0.5/MMBtu, what is the cost of production of the liquefied natural gas product?

E.6.6. Natural Gas Liquids Recovery

Natural gas typically contains a range of hydrocarbon compounds, as well as carbon dioxide and hydrogen sulfide. Ethane, propane, and butane are often recovered from natural gas for use as petrochemical feed stocks. Typical recovery processes are described in U.S. 4,157,904, assigned to Ortloff Corp. Estimate the cost of recovering ethane and producing a natural gas product that meets pipeline specifications for a plant that processes 150 MMscfd of natural gas with the feed composition given in Example 3 of the patent. Assume the feed also contains 480 ppm of H_2S, 14 ppm of COS, and 31 ppm of methyl mercaptan.

E.7. INORGANIC CHEMICALS

E.7.1. Ammonia

Ammonia is an important basic chemical and is the starting point for most fertilizer manufacture. A conventional ammonia production process is described in U.S. 4,479,925, assigned to M. W. Kellogg. U.S. 5,032,364 (assigned to ICI) describes a more heat-integrated process, while U.S. 6,216,464 (assigned to Haldor Topsoe A/S) describes a process with power recovery. Estimate the cost of production via each route for a new plant on the U.S. Gulf Coast and for a plant fed with natural gas from a remote gas field in a developing country that is priced at $0.50/MMBtu. Does the price of the natural gas affect the selection of optimum process?

E.7.2. Bromine

Bromine can be produced by reacting bromide-rich brines with chlorine. The purification of the resulting gas mixture is described in U.S. 3,642,447 (unassigned).

If a brine solution containing 0.2 wt% NaBr and 3.4 wt% total salts can be extracted from a well at a cost of $4/metric ton, then would it be economical to produce bromine from this brine?

E.7.3. Fischer-Tropsch Catalyst

The Fischer-Tropsch process is a means of converting synthesis gas into hydrocarbons (see problem E.6.1). The manufacture of a catalyst for this process is described in U.S. 6,130,184 (to Shell Oil Co.). Estimate the cost of production of this catalyst.

E.7.4. Nitric Acid

Nitric acid is made by catalytic oxidation of ammonia. U.S. 5,041,276 (to ICI) gives selectivity data for various catalysts and process conditions. Determine the optimal catalyst and conditions to minimize the cost of production.

E.7.5. Urea

Urea is used as a fertilizer and is made by reacting ammonia with carbon dioxide. The reactions essentially proceed to equilibrium, but the process must be designed to minimize emissions of ammonia. The urea is usually formed into a solid product by prilling. U.S. 6,921,838 (to DSM B.V.) describes a novel process for urea production. Estimate the cost of producing ammonia via this route. Assume that carbon dioxide is available as a byproduct of the ammonia plant (see problem E.7.1).

E.7.6. Zeolite Synthesis

Synthetic zeolites are used in a variety of catalyst and adsorbent applications. Most zeolites are synthesized in batch processes, but U.S. 6,773,694 (to UOP) describes a continuous crystallization process for zeolite formation. The resulting crystals can be dried and formulated into catalysts, adsorbents, and other products. Estimate the costs of producing zeolite X and Mordenite by this method.

E.8. PHARMACEUTICALS

These problems are based on some of the highest volume and highest value pharmaceutical compounds at the time of writing. In most cases, the desired product is an active pharmaceutical ingredient (API), although a few of the problems relate to other compounds used in drug formulation.

Many of the high-value API compounds are formed in multistep syntheses starting from compounds that are themselves specialty chemicals. The patents that are cited give the preparation in the form of a laboratory recipe rather than a process flowsheet, and hence the chemist's recipe must be scaled up to the production recipe. A decision on whether to use batch or continuous production must also be made. These are therefore difficult design problems.

In most cases, the original preparation patent has been cited, as this may be the only route that has received FDA approval. A detailed patent search may reveal alternative routes that can be studied for comparison. Note that several of the products listed under food processing also have pharmaceutical applications, for example, as fillers, coatings, and sweeteners.

E.8.1. Acetaminophen

Acetaminophen (N-acetyl-p-aminophenol, paracetamol) is an analgesic marketed under a variety of brand names including Tylenol™, Calpol™, and Panadol™. Preparation of the API is described in U.S. 2,998,450 (to Warner Lambert). U.S. 4,474,985 (to Monsanto) describes a process for improving product quality and shelf life. U.S. 5,856,575 (to Council of Scientific Industrial Research) describes an alternative process. Estimate the cost of production by each route.

E.8.2. Alendronate

Alendronate (4-amino-1-hydroxybutane-1,1-biphosphonic acid) is a biphosphonate drug used to treat osteoporosis and Paget's disease. U.S. 4,621,077 to Istituto Gentili describes the preparation of the API. Estimate the cost of production of the API by the method of Example 3.

E.8.3. Amlodipine Besylate

Amlodipine (4-(2-chlorophenyl)-2-[2-(methylamino)ethoxymethyl]-3-ethoxycarbonyl-5-methoxycarbonyl-6-methyl-1,4-dihydropyridine) is an antihypertensive, marketed as Norvasc™. U.S. 4,572,909 assigned to Pfizer Inc. describes the preparation of the API and several of the required precursors. Estimate the cost of production of the API.

E.8.4. Aspirin

Aspirin (acetyl salicylic acid) is a well-known analgesic. Processes for preparing aspirin are described in U.S. 3,235,583, U.S. 3,373,187 (both to Norwich Pharmacal), and U.S. 2,890,240 (to Monsanto). Estimate the cost of production by each route.

E.8.5. Aspirin (slow release)

Slow-release versions of aspirin for long-term use as an anti-inflammatory drug are described in U.S. 5,855,915. Estimate the cost of production of each of the slow-release formulations given.

E.8.6. Ciprofloxacin

Ciprofloxacin (1,4-dihydro-1-cyclopropyl-6-fluoro-4-oxo-7-(1-piperazinyl)-3-Quinoline-carboxylic acid) is a fluoroquinolone antibiotic drug used mainly to treat respiratory infections and septicemia. It also enjoyed a brief period of notoriety in 2001 as the preferred antibiotic for treating anthrax. Bayer's patent U.S. 4,670,444 describes the synthesis of the API and several of the required precursors. Estimate the cost of production of the API.

E.8.7. Citalopram Hydrobromide

Citalopram (1-[3-(Dimethylamino)-propyl]-1-(4-fluorophenyl)-1,3-dizohydro-5-iso-benzo-furancarbonitrile) is an antidepressant marketed as Celexa™. The original preparation is described in U.S. 4,136,193 (to Kefalas) and an improved route is given in U.S. 4,650,884 (to H. Lundbeck A/S). What is the saving in cost of production of the API by the new route?

E.8.8. Clopidogrel

Clopidogrel is an antithrombotic marketed as Plavix™. Preparation of the API is described in U.S. 4,529,596 (assigned to Sanofi), which also gives several pharmaceutical formulations of the drug. Estimate the cost of production of the API. What composition would you recommend for the tablet formulation, and what is the final cost of production for the tablet form?

E.8.9. Cyclosporin A

Cyclosporins are a group of cyclic nonpolar oligopeptides that are immunosuppressants and are produced by *Tolypocladium inflatum Gams* and other fungi. U.S. 4,117,118 gives details of the fermentation and product recovery. Estimate the cost of production and determine which species is preferred.

E.8.10. Doxycyline

Doxycycline (α-6-deoxy-5-oxytetracycline monohydrate) is an antibiotic. U.S. 3,200,149 (to Pfizer) describes the preparation of the API and several formulations. Estimate the cost of producing the tablet formulation given in the patent.

E.8.11. Fexofenadine

Fexofenadine is an antihistamine and is the API for Allegra™ and Telfast™. U.S. 4,254,129 (to Richardson-Merrell) describes the preparation of the API and several formulations of the product, including an aerosol solution (Example 11). Estimate the cost of production of the API and the 15 ml aerosol product.

E.8.12. Fluconazole

Fluconazole (2-(2,4-difluorophenyl)-1,3-bis(1H-1,2,4-triazol-1-yl)-propan-2-ol) is an antifungal. U.S. 4,404,216 assigned to Pfizer describes two methods for preparation of the API. Estimate the cost of production of the API by both routes and hence determine which is preferred.

E.8.13. Fluoxetine Hydrochloride

Fluoxetine (N-methyl-3-(p-trifluoromethylphenoxy)-3-phenylpropylamine) is an antidepressant. U.S. 4,626,549 (to Eli Lilly & Co.), U.S. 6,028,224 (to Sepracor), and U.S. 6,677,485 (to Ranbaxy) all describe different synthetic routes to this product. Which has the lowest cost of production?

E.8.14. Fluticasone Propionate

Fluticasone propionate is an antiallergic drug marketed as Flovent™. U.S. 4,335,121 (assigned to Glaxo) describes the preparation of the API. Estimate the cost of production of the API.

E.8.15. Granulocyte Colony-Stimulating Factor

Granulocyte colony-stimulating factor (G-CSF) is a hematopoietic stimulant (i.e., encourages formation of new blood cells and is given to patients who have undergone chemotherapy, bone marrow transplants, etc.). It can be produced by expression from genetically modified *E. coli*, as described in U.S. 4,810,643 Example 7. Estimate the cost of production of hpG-CSF using the method of this example.

E.8.16. Guaifenesin

Guaifenesin (Guaiacol glyceryl ether, 3-(2-Methoxyphenoxy)-1,2-propanediol) is an expectorant that is found in cough medicines such as Actifed™ and Robitussin™. U.S. 4,390,732 (to Degussa) describes preparation of the API and several of its precursors. Estimate the cost of production of the API.

E.8.17. Ibuprofen

Ibuprofen (2-[4′-isobutylphenyl]propionic acid) is a well-known analgesic marketed as Motrin™, Advil™, and other brands. U.S. 3,385,886 (to Boots Drug Co.) describes the preparation of the API and several formulations. Estimate the cost of production of the tablet form.

E.8.18. Lansoprazole

Lansoprazole is the API for Prevacid™, a treatment for gastric ulcers. U.S. 4,689,333 (to Takeda Chemical Industries) describes the synthesis of the API and the required precursors. Estimate the cost of production of the API.

E.8.19. Lisinopril

Lisinopril (N-(1(S)-carboxy-3-phenylpropyl)-L-lysyl-L-proline) is an antihypertensive. The preparation of the API and several product formulations are described in

U.S. 4,374,829 (to Merck & Co.). Estimate the cost of production of the API and the tablet formulation.

E.8.20. Loratadine

Loratadine (11-[N-carboethoxy-4-piperidylidene]-8-chloro-6,11-dihydro-5H-benzo-[5,6]-cyclohepta-[1,2-b]-pyridine) is an antihistamine. U.S. 4,282,233 (to Schering) describes the preparation of the API and also gives recipes for syrup (Example 6) and tablet (Example 7) formulations. Estimate the cost of the making the API and both formulations.

E.8.21. S-Ofloxacin

S-Ofloxacin is an optically active fluorinated quinolone with antibacterial properties. U.S. 5,053,407 describes the preparation of the API. Estimate the cost of production of this compound. Which stages of the process would you operate in batch mode and which stages would you operate continuously?

E.8.22. Omeprazole

Omeprazole (5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole) is an antiulcerative marketed as Prilosec™. The preparation of the API in unresolved form is described in U.S. 4,255,431 and U.S. 4,508,905 (both to AB Hässle), while U.S. 5,693,818 (to Astra) describes a route for preparing the optically pure enantiomers. Estimate the cost of producing the S-form by each method.

E.8.23. Paroxetine

Paroxetine is an antidepressant marketed by GlaxoSmithKline as Paxil™. Example 2 of U.S. 4,007,196 (to A/S Ferrosan) describes preparation on the free base from of paroxetine, while U.S. 4,721,723 (to Beecham Group Plc.) describes the synthesis of the crystalline hydrochloride hemihydrate, which is the preferred form to administer the drug. What is the cost of production of the API in the crystalline hydrochloride hemihydrate form?

E.8.24. Pseudoephedrine

Pseudoephedrine (2-methylamino-1-phenylpropan-1-ol) is a nasal decongestant. U.S. 4,277,420 (to Monsanto) describes the preparation of the API and several possible precursors. Estimate the cost of production of each route and determine which route is cheapest.

E.8.25. Risperidone

Risperidone (3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one) is an antipsychotic marketed by Johnson & Johnson as Risperdal^{TM}. The preparation of the API and several formulations are described in U.S. 4,804,663. Estimate the cost of making the API and the tablet and injectable solution formulations.

E.8.26. Sertraline Hydrochloride

Sertraline (cis-(1S)-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthaleneamine) in the hydrochloride salt is an antidepressant marketed as Zoloft^{TM}. U.S. 4,536,518 (to Pfizer, Inc.) describes the preparation of the API. Estimate the cost of production of the API.

E.8.27. Simvastatin

Merck & Co. patent U.S. 4,444,784 describes the process for synthesizing simvastatin, which is the API for Zocor^{TM}, a cholesterol-lowering drug. Flowsheet A in the patent gives several possible routes to make the API. Which is the lowest cost?

E.8.28. Sumatriptan

U.S. 4,816,470 assigned to Glaxo describes the process for making 3-(2-Aminoethyl)-N-methyl-1H-indole-5-methanesulponamide, which is the API for Imigran^{TM}. Estimate the cost of production for a generic manufacturer to produce this compound.

E.8.29. Venlafaxine

Venlafaxine (1-[2-(Dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol) is an antidepressant marketed as Effexor^{TM}. Synthesis of the API is described in U.S. 4,535,186 assigned to American Home Products. Estimate the cost of production of the API.

E.9. PULP AND PAPER

E.9.1. Biopulping

Biological pretreatment has been suggested as a means of improving both mechanical and Kraft pulping. U.S. 6,402,887, assigned to Biopulping International, describes a biological treatment process for wood waste that leads to paper of comparable quality to that produced with virgin wood. Estimate the cost of the biological pretreatment step per pound dry mass of paper product. At what price (recovery cost) of wood waste would this process deliver a 12% internal rate of return?

E.9.2. Black Liquor Recovery

Black liquor is a byproduct produced in the Kraft process for paper pulping (see problem E.9.5). Black liquor has a high content of organic compounds and salts and is often incinerated to provide part of the site fuel requirement. U.S. 6,261,411 (unassigned) describes a process for recovery of chemicals from black liquor. Estimate the net present value of a plant that used this technology in a world-scale paper mill.

E.9.3. Chemimechanical Pulping

U.S. 4,900,399 (to Eka AB) and U.S. 5,002,635 (to Scott Paper Co.) both describe chemical pretreatments that claim to improve the properties of mechanical pulp. Estimate the cost of these pretreatment processes for a world-scale mechanical pulping plant. Which method would you recommend?

E.9.4. Chlorine-Free Bleaching

Methods of bleaching paper pulp with reduced consumption of chlorine chemicals are of interest to the paper industry, as they reduce the environmental impact of paper manufacture. U.S. 5,004,523 (to U.S. Dept. of Agriculture) and U.S. 5,091,054 (to Degussa) describe a pulp pretreatment using Caro's acid that enhances oxygen delignification and peroxide bleaching. Estimate the cost of this treatment (including the cost of processing any waste streams generated) for a typical Kraft paper mill.

E.9.5. Kraft Pulping

The Kraft process is used for production of pulp for high-quality paper. Improvements to the Kraft process are described in U.S. 5,507,912 (to H. A. Simons Ltd.) and U.S. 7,097,739 (to Solutia Inc.). Estimate the annual savings gained by each of these processes relative to conventional Kraft pulping.

E.10. SPECIALTY CHEMICALS

E.10.1. Acetophenone

Acetophenone (phenyl methyl ketone) has a wide range of applications in perfumery. It can be recovered from the heavy byproduct stream of a phenol process (which otherwise has fuel value) using the process described in U.S. 4,559,110 assigned to Dow Chemical. It can be made by oxidation of ethylbenzene using the process described in U.S. 4,950,794 (to Arco Chemical Technology). It can also be produced as a "natural" product by fermentation of cinnamic acid using the process described in U.S. 6,482,794 (to International Flavors & Fragrances). Estimate the cost of production via each route.

E.10.2. Carbon Nanotubes

Carbon nanotubes are of current interest as a novel material that can be used in a variety of applications. Large-scale use of these materials has been hindered by the absence of a process that can produce large quantities of high-purity product. U.S. 6,413,487 (to University of Oklahoma) describes a process for large-scale production of single-wall carbon nanotubes. U.S. 6,333,016 (also to University of Oklahoma) gives yield data. U.S. 5,560,898 (to Agency of Industrial Science and Technology, Japan) and U.S. 5,641,466 (to NEC Corp.) describe processes for separating nanotubes from graphitic carbon. U.S. 5,698,175 (to NEC Corp.) describes a process for purifying and uncapping carbon nanotubes. Develop a flow scheme for production of high-purity single-walled carbon nanotubes and estimate the cost of production.

E.10.3. 3-R Citronellol

3-R citronellol is a fragrance. U.S. 4,962,242 (to Takasago Perfumery Co) describes a preparation from geraniol (Example 2). Estimate the cost of production.

E.10.4. Cleve's Acid

1,7-Cleve's acid (1-naphthylamine-7-sulfonic acid) is used in dye manufacture. The preparation is described in U.S. 2,875,243 (to Bayer). Estimate the cost of production.

E.10.5. Dextrins

Dextrins are used in making pills, bandages, paper, fabrics, glue, matches, and a range of other applications that require thickening of pastes. They are made by enzyme hydrolysis of starch, as described in U.S. 6,670,155 (to Grain Processing Corp.). Estimate the cost of producing and purifying dextrin with recovery of the retrograded amylose.

E.10.6. D-Malic Acid

Malic acid (hydroxybutanedioic acid) is a chemical intermediate and is also used as a food flavor enhancer. It can be made by several routes. U.S. 5,210,295 (to Monsanto) describes a nonenzymatic process. U.S. 4,772,749 (to Degussa) describes recovery of malic acid from the product of enzymatic conversion of fumaric acid. U.S. 4,912,042 (to Eastman Kodak) describes an enzymatic separation process for separating the *L*- and *D*-isomers. U.S. 5,824,449 (to Ajinomoto Co.) describes a selective fermentation from maleic acid. Estimate the cost of production of *D*-malic acid by each process and determine which is cheapest.

E.10.7. Salicylic Acid USP

Salicylic acid is used as a raw material for making aspirin, as well as a starting material for dyes and as a pharmaceutical compound. It is made by heating sodium phenolate with carbon dioxide under pressure, and the process is described in several of the standard reference works listed in Chapter 8. Estimate the cost of production.

E.11. WASTE TREATMENT AND RECOVERY

E.11.1. Nylon Recycling

Waste carpet typically contains large quantities of Nylon 6, which can be converted back into caprolactam. Recycling processes are described in U.S. 7,115,671, U.S. 6,111,099 (both to DSM B.V.), and U.S. 5,359,062 (to BASF). Determine the economics of recovering caprolactam from carpet waste if the waste is available at a cost of $-30/metric ton (i.e., you are paid $30/ton to accept it). How does this compare to burning the waste carpet in an incinerator with a steam turbine cogeneration plant?

E.11.2. Sulfur Dioxide Treatment

Sulfur dioxide is formed whenever sulfur-containing fuels are combusted in air. Sulfur dioxide can lead to the formation of acid rain and is a controlled pollutant in most countries. U.S. 5,196,176, assigned to Paques B.V., describes a biological process for removing sulfur dioxide from a vent gas and converting it to elemental sulfur. Estimate the cost (in $/kWh) of using the Paques process to treat the flue gas from a 1000 MW power station that burns Illinois Number 6 coal in pressurized fluidized bed combustors.

E.11.3. Sulfur Recovery

Many processes release sulfur in the form of H_2S, which is highly toxic and must be converted to a marketable form such as elemental sulfur or a stable disposable product such as a sulfate salt. U.S. 5,397,556 (to Regents of the University of California) describes a process for converting H_2S to elemental sulfur. How does the cost of sulfur produced by this process compare with the cost of sulfur produced by the conventional modified Claus process?

E.11.4. Toxic Waste Disposal

A novel process for toxic waste handling is suggested in U.S. 4,764,282 (to Uniroyal Goodrich Tire Company). A waste liquid is soaked up into ground tire rubber to form a stable solid that can be transported with reduced risk of spillage. The resulting product can then be incinerated in a fluidized bed combustor, similar to the fluidized bed combustors used in coal-fired power stations. Estimate the cost of waste disposal via this route, allowing for a credit for the electricity produced. How does this compare to the cost of toxic waste disposal by conventional incineration?