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Eli Lilly and Company: The Flexible Facility Decision (1993)

In November 1993, Steve Mueller, manager of strategic facilities planning at Eli Lilly and Company, mulled over a difficult situation. Mueller had to make a recommendation to the company's Manufacturing Strategy Committee about the type of manufacturing facilities to construct for three new pharmaceutical products that the company expected to launch in 1996. The question about what *kind* of capacity to add for these three products had touched off a broad debate within the company about manufacturing strategy at Lilly.

In the past, Lilly had built a variety of types of facilities for new products. Some of these were dedicated to a single product, while others were designed to produce a specific set of products. Plants were considered "specialized" because they could only manufacture products for which they were specifically designed. Construction would begin as soon as the company was reasonably certain that the product would be commercialized, usually two to three years before product launch. The strategy had worked well in the past, but in the increasingly competitive marketplace of the 1990s, some believed that the company needed to revise its approach. Lilly's top management had set stringent goals to increase new product speed to market and to reduce the cost of manufacturing. The facilities strategy would have to be aligned with these goals.

One alternative to the current strategy was to build flexible manufacturing facilities which could accommodate virtually any of Lilly's new products. A facility of this type could suit all three of Lilly's new products and could serve as a "launch plant" for future new products. The concept was attractive for a number of reasons. In the past, there were cases in which the time required to design and build a specialized plant had delayed the launch of new products. Late changes in the process technology for a particular product were also difficult to accommodate after specialized equipment was already installed. In addition, specialized plants entailed risk. Because plant construction had to begin well before the end of clinical testing, there was always the risk that the plant would be idle if there was a delay in the regulatory approval. Even worse, if a drug never made it to market, the plant would have to be retrofitted for another product. Nevertheless, the flexible plant strategy was not without its drawbacks. For example, flexible plants were much more costly to build and operate than specialized plants. While Mueller was attracted to the flexible plant concept, a number of questions raced through his mind. Could the higher capital costs of the flexible plant be justified on financial grounds in the increasingly competitive environment Lilly faced in the 1990s? How did it fit with new corporate goals of faster time to market and manufacturing cost reduction? Were there alternatives no one had yet identified? Steve Mueller wanted to have these questions answered in his own mind before making a recommendation to the Manufacturing Strategy Committee.

Professor Gary Pisano and Research Associate Sharon Rossi wrote this case as the basis for class discussion rather than to illustrate either effective or ineffective handling of an administrative situation. Some data have been disguised.

The Pharmaceutical Industry in 1993

In 1993, sales of ethical pharmaceuticals (prescription drugs) totaled $191 billion worldwide. While there were hundreds of companies in the industry, the top 15 competitors accounted for more than one-third of industry sales worldwide. In the United States, the world's single largest market, the four largest companies, Merck, Bristol-Myers Squibb, SmithKline Beecham, and Eli Lilly, accounted for 25% of the $50 billion in drug sales. Outside the United States, major markets included Japan (with an estimated 13% market share), Germany (6%), France (5%), Italy (5%), and the United Kingdom (3%).

One of the most critical activities for pharmaceutical companies was the discovery and development of novel therapeutic compounds. Companies' research laboratories typically screened thousands of chemical compounds in search of ones that had potential for treating or curing disease. Once a compound was shown to have therapeutic potential, it typically took a company eight to twelve years to develop it into a marketable product. This long process included first testing the product for biological activity and toxicity in the laboratory, testing for safety and efficacy in three phases of human clinical trials[1], developing a process for commercially manufacturing the product, designing an appropriate dosage strength and formulation (i.e. tablet, capsule, liquid, etc.), and submitting the product for approval by federal regulatory agencies. In the United States, New Drug Applications (NDAs) were submitted to the Food and Drug Administration (FDA) for review. The fall-out rate of new drugs in development was extremely high. According to one study, of every 10,000 chemical compounds synthesized in the laboratory, only 10 could be expected to enter human clinical trials, and of these, only 1 would make it to market.[2]

In addition to the uncertainty about whether a product would be approved, there was uncertainty about the amount of a new drug that would be required for the market. Volume depended on a drug's potency and side-effect profile (which were determined during clinical studies) and market demand (which could only be estimated prior to launch). For a typical product, production volumes started relatively low in launch year, increased over time, and peaked at about the fifth year of commercial sales. A drug's 17 year patent usually ran out after the tenth year, so that sales tapered off as lower-priced generic substitutes became available.

Once on the market, pharmaceutical products were sold to hospitals, health maintenance organizations (HMOs), retail pharmacies, and physicians, each of which prescribed the drugs to patients. In hospital sales, the hospital pharmacy and therapeutics committee decided what products the hospital would stock. At HMOs, the buying decisions were similar, but these organizations were usually more cost-conscious. Three-fourths of the sales volume of ethical pharmaceuticals were sold to wholesale distributors. One-fourth of the volume was sold directly to hospitals, HMOs, retail pharmacies, and physicians.

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[1] Phase I clinical trials determined the safety and pharmacological properties of a compound, by conducting tests on 20 or more healthy volunteers. Phase II clinical trials evaluated the effectiveness of a drug and isolated side effects. Phase II tests were typically conducted on several hundred (volunteer) patients. Phase III clinical trials measured the drug's effect on a large sample of patients (typically thousands of patients) over several years. Phase III trials determined the long-term side effects and provided information on the effectiveness of a range of doses administered to a mix of patients.

[2] Sheck, L. (1984) "Success Rates in the U.S. Drug Development System," *Clinical Pharmacology and Therapeutics*, vol. 36, no. 5: 573-583.

Changes in the Industry Environment: "A New Marketplace"

The U.S. pharmaceutical industry had historically been one of the most profitable and fastest growing sectors in the U.S. economy. The average annual growth rate was 18% during the period 1982 through 1992, but was expected to slip to the 8% to 12% range in 1993 and beyond. Throughout the 1970s and 1980s, pharmaceutical company earnings and return-on-equity grew at a double-digit pace, fueled by many new product developments, strong patent protection, and pricing flexibility in the United States. Although sales volume declined by 15% since 1987, many companies were able to maintain revenue and earnings growth by raising prices.[3] Traditionally, average gross margins on products ranged from 70% to 85% in the U.S. and 60% to 70% in Europe.

Beginning in 1991, the pharmaceutical industry environment began to change. A set of new factors were at work that put pressure on drug margins from multiple directions: pricing flexibility was diminishing, the rate of innovation was slowing, competition within drug classes and from generic substitutes was growing. Investors acknowledged the negative impact of these changes, as pharmaceutical stock prices declined by 35% between 1991 and mid-1993.

Beginning in the late 1980s, the rate of new drug innovation began to slow throughout the industry. Even though most companies had dramatically increased the amount invested in R&D, development pipelines at companies were no longer deep with promising new compounds. Industry-wide, pharmaceutical companies were investing more in R&D—total R&D expenditures grew from $1.1 billion in 1975 to an estimated $12.6 billion in 1992—but the number of novel drug compounds launched during this period had risen only slightly.[4] Due to increasing regulatory requirements and the complexity of new compounds, the cost of developing drugs was also increasing. According to one study, the cost to develop a new drug was estimated to be $359 million in 1992 (taking into account the cost of the many compounds that never made it to market), up from $120 million 5 years earlier.[5]

The cost of manufacturing pharmaceuticals was also increasing. In the 1990s, manufacturing costs represented about 20% of sales, up from 10% in the early 1980s.[6] According to one forecast, the average cost of goods as a percentage of sales in the industry was expected to increase to 60% by the year 2000. There were several reasons for the escalating costs of manufacturing. In the United States, more stringent FDA regulations concerning product quality[7] required drug companies to invest in more sophisticated production equipment while Environmental Protection Agency (EPA) regulations were forcing them to invest in costly pollution control equipment and waste treatment facilities. Many new drugs were based on highly potent compounds and production of these required investment in costly containment facilities. In addition, as drug discovery and design technology advanced, drug researchers were able to synthesize more complex molecules in the laboratory; these complex molecules typically required more advanced production technology for large scale manufacturing. Finally, the increased cost of manufacturing was also attributed to under-utilization

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[3] Manufacturers of ethical pharmaceuticals received a 132% increase in prices (as measured by the Producer Price Index) during the 1980s, compared with the overall inflation rate of 22% for all finished consumer goods. (*Medical and Healthcare Marketplace Guide*, 1993 (9th edition), MLR Biomedical Information Services, p.36)

[4] The number of new molecular entities (compounds with chemical structures different from those already on the market) approved by the FDA increased from 22 in 1984 to 26 in 1992, with a median of 23 compounds per year. (Standard & Poor's Industry Surveys, 9/9/93, p. H25.)

[5] *Pharmaceutical R&D: Costs, Risks, and Rewards*, U.S. Office of Technology Assessment, February 1993.

[6] "A Modern Smokestack Industry," *The Economist*, November 1992.

[7] Although regulations about quality were becoming more explicit, product quality was a "given" in this industry. All pharmaceutical companies' products were at least 99.8% pure.

of facilities throughout the industry. These increases were forcing companies to focus for the first time on the cost of manufacturing and the cost of manufacturing capacity.

Several other factors were at work that limited pharmaceutical companies' ability to recoup these escalating R&D and manufacturing costs through higher prices. One of these was government intervention. In 1993, the Clinton administration, in an attempt to curb the upwardly spiraling cost of health care, was proposing caps on price increases and caps on reimbursement for Medicare and Medicaid, measures which many people believed translated into federal price controls. It was uncertain how severely the federal policy would impact the drug industry, but it was clear that pricing flexibility would be diminished. By mid-1993, 17 of the leading U.S. pharmaceutical companies had voluntarily agreed to hold price increases on products to the Consumer Price Index.[8]

Potential government regulation was not the only force limiting pricing flexibility. Rapid growth of managed care providers was also having an impact. HMOs and other types of managed care networks represented an increasing share of health care providers, accounting for 64% of pharmaceutical purchases in 1992. This figure was expected to grow to 75% by 1995.[9] These and other large, centrally-administered customers were buying in bulk and often relied on formulary lists that limited purchases to only one or two drugs for a given condition, they were able to demand price discounts of as much as 60% from pharmaceutical companies. Third-party payers (including Medicare, Medicaid, and private insurers) were also gaining leverage on drug companies, as more and more included coverage of prescription drugs in their benefit plans. In 1991, 45% of prescription drug expenditures were funded by third-party payers, up from only 4% in 1960.[10]

Another factor pressuring drug margins was increased competition from the pharmaceutical companies themselves. More firms were working on developing similar compounds, making some therapeutic classes more crowded with potential substitutes. Mark Foglesong, executive director of manufacturing and facilities at Eli Lilly, described it this way: "Nowadays, everybody's playing in the same sandbox." The first drug of its kind to win approval set the market price and usually enjoyed a period of exclusivity before competing products were launched, but the period of exclusivity was shrinking. Foglesong added, "If you developed a blockbuster drug in the past, few firms were following on. Now, blockbusters have rapid followers." According to Peter Johnson, director of manufacturing planning at Eli Lilly,

> In the late '70s and early '80s, you could expect about five to six years of exclusivity before competitors launched a product with similar therapeutic effects. That window has been cut in half. For example, with *Prozac* [an anti-depressant], we only had the market to ourselves for a little more than two years.

This shorter period of market exclusivity meant not only lower sales, but allowed less time for a company to recoup its R&D investment. Second entrants in the market for a particular indication, although branded and patented, had to discount their prices (34% on average) to attract market share. These "me-too" drugs had the effect of reducing prices across all products within the therapeutic class.

Additional pricing pressure was coming from the growing availability and use of generic drugs. Generic products were essentially copies of branded and patented products whose patents had expired. In the 1990s, more generic drugs were becoming available, eroding sales of branded and patented products. In 1993, roughly half of all prescriptions in the United States were filled

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[8] Outside the United States, drug prices were generally regulated by government. However, the evidence was mixed whether such regulation actually led to lower drug prices.

[9] *Medical and Healthcare Marketplace Guide* (MLR Biomedical Information Services) (9th edition) 1993, p.34.

[10] Ibid.

generically, as compared with about 2% in 1980.[11] They were typically priced 30% to 60% lower than brand-name products. These lower prices could be charged because generic companies did not have to recoup R&D costs or sales and marketing expenses. In some cases, generics compelled pharmaceutical companies to drop their prices. Even when a company's own drug remained under patent protection, it could face price competition if a competitor's drug within the same therapeutic class came off patent and a generic version was introduced. It only took one generic entrant to subject the entire class of products to generic pricing pressure. Between 1993 and 1999, patents would expire on branded products with annual sales of $20 billion, and generic substitutes were expected to capture a significant share of these sales. There were few therapeutic areas free from generic competition. Analysts estimated that, by the year 2000, generic sales would triple to more than $12 billion, up from $4 billion in 1992.

As the period of market exclusivity decreased and price flexibility was reduced, companies began to understand the value of getting a new compound to market as quickly as possible, preferably before competitors. The value of getting a new drug to market one year sooner or one year later was equal to one year's net sales gained or lost. For a large market drug, one year's net sales could be as high as $175 million. To shrink time to market, companies were working on designing shorter clinical trials, the traditional "bottleneck" in the drug development process.

Eli Lilly and Company

Company Overview

Eli Lilly and Company, headquartered in Indianapolis, Indiana, developed, manufactured, and marketed pharmaceuticals, medical devices, diagnostic products, and animal health products. Total company sales were $6.2 billion in 1992. Sales of ethical pharmaceuticals were $4.5 billion that year, ranking Lilly ninth in the world among drug companies, with a 2.5% market share. In the United States, Lilly ranked among the top six pharmaceutical companies. Two products, *Ceclor*, an antibiotic, and *Prozac*, an anti-depressant, accounted for a large part of Lilly's pharmaceutical sales: *Ceclor* sold $950 million and *Prozac* sold $1.1 billion in 1992. Both were among the 15 biggest-selling drugs in the world. (See company financials in **Exhibit 1**.)

In the 1990s, Eli Lilly was faced with competing in "a new marketplace." *Prozac* was the world's number-one selling anti-depressant in 1993. Although sales were growing steadily, recently introduced competing products, including Pfizer's *Zoloft* and SmithKline Beecham's *Paxil,* were beginning to capture an increasing share of the anti-depressant market. Lilly's *Ceclor* went off patent in 1992 and was surpassed in the same year by SmithKline Beecham's *Augmentin* as the world's leading anti-infective. All of the company's existing products had therapeutic substitutes on the market, and no "blockbuster" products were far along in the development pipeline. In 1993, Lilly's profit margins were 22%, but were expected to fall to 15% by 1996.[12]

Facing these fierce market conditions, management at Lilly believed that the company needed to better focus on serving the needs of customers and bringing new products to market faster, at lower cost. A set of company-wide goals were established concerning time to market and manufacturing costs. It typically took Lilly between 8 and 12 years to develop and launch a new drug. Several initiatives were underway to reduce development leadtime by as much as 50%. Another goal was to reduce manufacturing costs by 25%.

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[11] Standard and Poor's Industry Surveys, 12/16/93, p. H4

[12] Nancy Hass, "Serious Medicine," *Financial World,* 11/9/93, p. 32.

Some people within Lilly believed that the company would have to make major changes in how it developed and manufactured products in order to meet these targets. For example, to meet a product launch target in 50% less time, the company would have to get manufacturing facilities ready for production much earlier than it had in the past. Bill Smith, executive director of engineering, explained,

> To meet this new launch goal, we'll need to have our facilities ready much earlier. The reality of getting facilities ready fast means you almost have to start designing your production facility while the product is still very early in development. You also have to know what the manufacturing process is at this early stage.

Mark Kamer, department head of process research and development, foresaw the need to change the way production processes were developed:

> Under the new approach, we'll have to do a lot of development very early. We will also have to finalize the manufacturing process much earlier even if this means we wind up with less than optimal yields.

Meeting the 25% cost reduction goal also posed a challenge. Ed Smithwick, vice president of biochemical manufacturing, noted,

> Twenty-five percent is a very big number considering that most of our costs of production are fixed. The only way to do it is to increase the volumetric efficiency of our existing plants so we can increase volumes without investing in more capacity.

Greg Davis, manager of finance, added:

> We can nickel-and-dime for a 5% cost reduction. To make a 25% reduction, you really need a big jump in utilization. You either need to figure out how to make manufacturing capacity more productive or you need to reduce your asset base. Traditionally, this has not been a high priority for the company.

Lilly's Existing Operations Strategy

Facilities and Capacity

Eli Lilly operated 23 plants worldwide, including four plants in Indiana. Plants in the network were of two types: 1) bulk drug manufacturing facilities and 2) formulation, filling, and finishing. Bulk chemical manufacturing produced the active chemical and biochemical ingredients for a drug while filling and finishing operations formulated the active ingredients into a pill, capsule, liquid, or other form. Of the 23 plants in Lilly's network, eight plants were for bulk chemical manufacturing and fifteen plants were for filling and finishing operations. Fill and finish operations were geographically dispersed around the world. Operations were located this way in order to achieve local market presence and because filling and finishing specifications for a product varied by market.[13] In many countries, trade barriers made it more attractive to fill and finish domestically. In contrast, production of a particular active ingredient ("bulk drug") was usually concentrated into one or two plants, both to achieve economies of scale in large volume and because the active ingredients in a product did not vary by market. In bulk drug manufacturing, each plant contained several

[13] For example, a product might be formulated as a liquid in some markets and a topical cream in others.

different production suites or facilities, each of which produced a specific product. Approximately 60% of Lilly's manufacturing assets were tied up in bulk facilities.

The process for making bulk drugs usually involved several different chemical steps, each of which took place in a different tank (sometimes called vessels or reactors). Ingredients were combined based on the chemical "recipe" in one tank, heated, mixed, or otherwise modified in the tank, then piped to another tank for another processing step, etc.[14] Tanks came in different sizes (typically 500 gallons to 4,000 gallons), with different controls, different temperature ranges, and different piping configurations.

In bulk drug production at Lilly, the standard unit of capacity was known as a "rig." A rig was the set of tanks and equipment required to process from start to finish 2,000 gallon batches. One of the challenges of capacity planning was that the output (in kilograms) of a rig varied by both the product and the particulars of the process technology. For example, for a very complex product, the amount of bulk drug produced from one rig might be only a few hundred kilograms. In contrast, another, much simpler product, might require only one rig to produce several thousand kilograms of bulk drug. Thus, in forecasting future capacity needs (in rigs), Facilities Planning had to take into account *both* the expected demand for a product (in kilograms) and the expected volumetric efficiency of the process (in kilograms per rig). In 1993, Lilly's products occupied about 12 rigs of capacity; by 2004, total capacity requirements were forecast to reach 46 rigs, assuming no changes in production technology and no process improvements. The smallest increment of capacity that could be built or added to an existing facility was one-quarter of a rig (or 500 gallon batches).

Bulk Drug Facilities Strategy

Historically, Lilly built a specialized facility or converted an existing one for each new product. In some cases, the company built multi-product facilites which were specialized for a specific set of products. All facilities, including single-product and multi-product plants, were for dedicated use, meaning they produced only those products for which they were designed. The type of equipment and size (capacity) of the facility were customized to the particular specifications of the product or set of products. For example, a single-product facility had specialized tanks, equipment, piping, and process controls that were configured to run the particular production process for a specific product. Because of the time and disruption to existing operations involved in adding physical capacity, new facilities were built to accommodate estimated peak demand for the product or set of products, which typically occurred five years after market launch. As a result, new facilities were typically underutilized for the first several years as product demand approached its peak. (See **Exhibit 2**.) In a multi-product plant, capacity could not be "swapped" among products; excess capacity for any one product could not be used to produce any other product.

A product stayed in its facility throughout its commercial life, which was usually about 15 years. In the past, demand for most products generally tapered off in about the twelfth year as both generic substitutes and newer, patented substitutes became available. As demand declined, the plant would again have excess capacity. At the end of the product's life, when Lilly would no longer manufacture the drug, the facility could be converted to produce another product. This changeover, referred to as a "retrofit," involved replacing tanks, equipment, piping, etc. and took about one year. During the changeover, the plant could not be used. The cost to retrofit was roughly equal to the cost to build a new facility.

In 1993, all of Eli Lilly's bulk drug commercial manufacturing plants were specialized. However, attempts had been made in the past to pursue a more flexible approach. Lilly had

[14] Production was not always continuous. In-process product was often stored in large drums between steps.

constructed some "generic" facilities that were not specialized for a product or set of products. Over time, though, these plants did not make production more flexible. According to Bill Smith,

> The flexible plant concept is really not new. In the past, we used to build plants that were capable of making a variety of products. But once a product was in, and volume began to increase, we would start to modify the equipment to improve yields, cycle times, and throughputs. What would start out as a flexible plant would gradually evolve into a specialized plant.

One of the chief concerns about the specialized facilities strategy was the time involved for design and construction. Because facilities were designed around specific products and processes, facilities engineering typically could not begin its work until process development activities were almost complete and the process technology was finalized. In addition, because a specialized facility could only manufacture one product, the company preferred not to start construction until there was a reasonably high probability that the product would make it to market. Unfortunately, this created severe time pressures in trying to launch new products. Art Morstadt, director of facilities delivery engineering, commented, "With the specialized plant, we're always under time pressure. There's always a crunch and facilities wind up on the critical path."

Bulk Drug Process Development

An integral part of bringing a new drug to market was developing a production process to manufacture the active ingredient. The challenges of process development had increased in recent years as molecules became more complex (and thus required more sophisticated process technology) and as the company sought to achieve large reductions in overall product development lead times. As Eldon Shuey, an executive director of Lilly Research Laboratories who was responsible for bulk process development in Indianapolis, commented: "Our goal is to get process development and availability of product for clinical trials off the critical path."

Lilly divided process development into three phases. (See **Exhibit 5**) In the earliest phase, the goal was to develop a crude process as quickly as possible in order to make the first several kilograms of bulk drug required to start clinical trials. As Eldon Shuey noted:

> The project can't move into Phase I clinical trials until we prepare enough material. We're rate limiting here. Our primary objective is to make enough material to get clinical trials started. Manufacturing cost and manufacturability are secondary issues we deal with later.

As a project progressed through clinical trials, it would become necessary to start developing a more manufacturable process. In the second phase of process development, chemists began to determine the sequence of chemical reactions which would be used in the manufacturing process. At the end of this second phase, the basic chemistry of the process would be "locked-down" (finalized) and process development activities would transfer from the Chemical Process Research group in Indianapolis to the Chemical Development group at Tippecanoe (located about two hours from Indianapolis). It was the job of the development group at Tippecanoe to undertake the final phase of development and refinement needed to make the process efficient and commercially viable at large scale. While Tippecanoe was a commercial manufacturing site, it also housed Lilly's larger scale pilot production facilities. This final stage of process development typically began during Phase III clinical trials and ended with the transfer of the process to the commercial manufacturing site.

Striving to reduce time-to-market, Lilly planned to significantly shorten the clinical timeline and would need to finalize the manufacturing process much earlier than it had in the past. In order to allow time for facilities to be designed and constructed, management expected that the final stage of process development would have to begin in Phase II clinical trials, instead of Phase III.

Sourcing

At Lilly, bulk chemicals requirements were met both through in-house production and through outsourcing. For a typical bulk drug, the company might outsource some of the steps of the chemical process, mostly those which were relatively simple and non-proprietary. Steps which were complex and proprietary (usually the final steps of the chemical process) were performed in-house.

Lilly considered its manufacturing capabilities to be an important competitive strength. The company believed that manufacturing in-house was critical for maximizing speed to market, assuring product quality, and guarding proprietary technology. It was also critical in impeding competitors. For example, *Ceclor*, one of Lilly's biggest-selling products, had to be produced in large volumes and required a very complex manufacturing process. The product went off-patent in 1992, but the company's expertise in manufacturing it gave Lilly an extra year of market exclusivity, since no generic manufacturer was capable of making it at a competitive price. With increasing excess chemical capacity in both the fine chemical industry and the pharmaceutical industry, Lilly was considering whether to outsource more of the process steps for older products.

Production Planning

In 1993, Lilly manufactured 13 different active ingredients in its bulk chemical and biochemical manufacturing facilities.[15] The scheduling of production took into account product demand, inventory levels, and production start-up and shut-down costs. The object of production scheduling was to optimize these three factors. For the most part, production runs were scheduled to maximize utilization. This meant long production runs, with interruptions only for scheduled maintenance. When a product was in the early or late years of its life, when sales volume was well below capacity, production runs might only be carried out during part of the year.

Because of the high gross margins of most products, however, it was absolutely critical that sufficient inventory be available. As one production scheduler described: "Although production scheduling seems quite complicated, it's really come down to a pretty simple dictum: Never stock out!" For this reason, the company carried a large inventory of finished bulk active ingredients.

Production scheduling was expected to get more challenging in the future for several reasons. In line with its new strategy, Lilly was hoping to dramatically increase the number of new products launched during the next decade. By the year 2004, the company could be producing as many as 37 active chemical ingredients. However, the nature of these products would be very different than those Lilly currently produced. Following a broad trend in the pharmaceutical industry, Lilly's new products were likely to be based on much more potent molecules. Because high potency molecules were used in much smaller dosage strengths, their production volumes were relatively low compared to Lilly's current products. At the same time, they actually consumed more manufacturing capacity per unit of output because they were typically more difficult to manufacture than older products. Because they were high value-added products, the high potency products of the future would be much more costly to keep in finished goods inventory.

The Manufacturing Facilities Decision

Alfatine, *Betazine*, and *Clorazine* were three products in development at Eli Lilly in 1993. Although there was still some uncertainty about whether they would receive FDA approval, the

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[15] Since each active ingredient could be formulated in a wide variety of ways (e.g. tablet, liquid, capsule, cream, ointment, etc.) and in a wide range of dosage strengths (e.g. 25 mg, 50 mg, 100 mg, etc.), the actual number of *final products* stocked by the company ran into the thousands.

company anticipated launching the three new products in 1996. In 1990, Lilly's facilities planning group submitted a proposal to Steve Mueller describing the new facility for *Alfatine*. Mueller recalled:

> *Alfatine* was in Phase I clinical trials and the engineering group began to design a specialized plant for it. At this stage, the process development people began to warn us that the manufacturing process might change. Because of the *Loracarbef* project, they really hadn't had much time for *Alfatine*. As a result, the process was still very immature. We realized we needed to keep some flexibility in the design of the new facility. The need for manufacturing process flexibility for *Alfatine* led to broader discussion about whether we should be using flexible facilities for all our new products.

By the end of 1993, a final decision needed to be made regarding what *kind* of capacity to add for the three new products and beyond: *Should Lilly follow its current strategy of building specialized facilities or should flexible facilities be constructed?* To make this decision, Steve Mueller analyzed the input he had gotten from people in operations, finance, marketing, and facilities planning (shown in **Exhibit 3**), keeping in mind the importance of meeting the goals for a 50% shorter development cycle and a 25% reduction in costs. Mueller laid out two options and considered the costs and implications of each.

Option 1: Build One Specialized Facility

Following the current strategy, Lilly would design and build one specialized facility for the three new products. In this plant, *Alfatine*, the largest-volume product, would have one full rig of capacity. *Betazine* and *Clorazine* would each have one-fourth rig of capacity, the minimum feasible scale for a facility.[16] All three products would remain in the facility throughout their 15 year lives. The total cost of building this three-product facility was estimated to be $37.5 million (Lilly depreciated manufacturing facilities over a 15 year period). Operating costs for the facility were expected to be $6.8 million per year. See **Exhibit 3** for a break-down of the capital and operating costs.

In the specialized facility, productivity per unit of capacity would be relatively high, averaging 16,000 kilograms of output per rig at 80% utilization. High productivity would occur because plant was specifically designed and optimized for the set of products, resulting in better yields. Operators would become experienced in running the processes, resulting in fewer problems or batch failures. With dedicated equipment and operators, more learning would take place, so the plant would have a steeper experience curve. The absence of product changeovers would result in a smoother operation of processes overall. See **Exhibit 4** for a schedule of demand and capacity.

However, building this type of facility would entail some risks. If any one of the products did not make it to market, part of the facility might have to be retrofitted to produce another product. If a manufacturing process was dramatically changed after construction had begun, a part of the facility might need to be redesigned or re-equipped to suit the new process. Since establishing the goal of 50% reduction in time-to-market, this risk was especially high. In order to meet the launch target, the facilities concept and design phase would have to begin about three months before final manufacturing processes were designed. (See **Exhibit 5**.) Construction would have to begin about 100 days before final product decisions were made. If the facility was not completed on schedule, a product launch could be delayed by weeks or months, costing millions of dollars in lost sales.

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[16] Lilly also considered putting the new products into 3 single-product facilities, but because Betazine and Clorazine were small volume products, a single three-product was more economical. Three single-product facilities would have significantly higher operating costs than one multi-product facility.

Option 2: Build One Flexible Facility

Under this option, Lilly would build one flexible facility. Like the specialized plant, the flexible facility could produce all three of the new products. However, it would also have the capability to produce virtually any new bulk chemical product, and could be used as a launch plant for future new products.[17] The cost of building this flexible facility would be $150 million and annual operating costs were estimated to be $9.48 million. See **Exhibits 3 and 4**.

There were two reasons why the flexible facility would cost so much more (nearly three times as much) than the specialized facilities to construct. One reason was related to the relatively lower productivity of flexible capacity and thus the need to install more capacity in the flexible plant to meet volume requirements for the three products. Because specialized facilities used equipment and procedures which were optimized for a particular product, and because operators were able to develop in-depth knowledge of the process over time, a rig of specialized capacity could produce 20,000 kilograms of product in a year. In contrast, a rig of flexible capacity could only produce a maximum of 7,500 kilograms of product in a year. This difference in productivity was further exaggerated by significant differences in utilization rates. Because the flexible plant would produce multiple products, change-over time between products would consume some available capacity.[18] The expected utilization of the flexible plant would be 65% compared to 80% for a specialized plant. [19] Taking into account utilization rates, a rig of flexible capacity could actually only produce 4,875 kilograms of product per year, whereas a specialized rig would yield 16,000 kilograms. Given these differences in productivity and utilization rates, the flexible facility would need three rigs of capacity to meet initial volume requirements for *Alfatine*, *Betazine*, and *Clorazine*. In contrast, the total capacity of three specialized facilities would only require 1.5 rigs.

Not only did the flexible facility require more rigs, but each flexible rig was also more costly to build than specialized capacity ($50 million per flexible rig versus $25 million per specialized rig). Higher cost per rig was the result of various factors. In a flexible factory, tanks were made of complex alloys or lined with glass (rather than stainless steel) so that they could handle all different types of reactions and materials without corroding. The facility would have a wider range of controls (for temperature, pressure, etc.) and flexible piping, which could be changed to suit different process technologies and process flows. In addition, the flexible facility would also have to stock relatively exotic pieces of equipment, just in case they were needed for a particular process. Finally, the plant had to be designed with empty floor space so that equipment could be changed around or new pieces of equipment could be added without disrupting existing operations.

The flexible facility could produce *Betazine* and *Clorazine* for their entire product lives. *Alfatine* would be launched in the flexible plant, but demand for this product was expected to exceed the capacity of the flexible plant by 2001. Based on current demand and yield projections, *Alfatine* would require its own specialized one-rig plant in 2001. A decision could be made later whether to build a new plant, retrofit an old one, or keep the product in the flexible facility, based on actual demand and process yield improvements. If *Alfatine* did move to a specialized plant, other new products could be produced in the flexible facility. Subsequent products would be produced for two

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[17] A "market entry plant" or "launch plant" manufactured new products temporarily, typically for two to three years after launch. After this period of time, products were moved into their own dedicated manufacturing facilities.

[18] An average of four product campaigns would be run each year (each 11 weeks long), with 2 weeks of down time between each campaign for cleaning, repairs, and maintenance.

[19] However, the flexible plant's utilization rate would not vary with product life cycles as was the case for specialized plants. Once the flexible plant was operating, there was expected to be enough volume to keep it at 65% utilization.

to three years in the flexible facility, then moved to specialized facilities as demand increased.[20] Forecasts indicated that there would be more than enough demand to fully utilize (up to 65%) the flexible facility.[21] In fact, if Lilly were to go with the flexible launch plant strategy, it would likely need to build several more flexible plants over the next 10 years to accommodate demand for new products. (See **Exhibit 6**.)

In spite of having lower yields and utilization, the flexible facility offered some significant advantages. Since a flexible facility was more adaptable, processes for making new products did not have to be finalized early in the concept and design phase of construction, as they did for a specialized plant. Mark Kamer commented, "The great thing about the flexible plant is that since design and construction of the facility are no longer issues, we can work on the process longer, without worrying about delaying the product launch."

Another advantage of the flexible plant was reduced lead-time for manufacturing new products. "The flexible plant takes facilities construction off the critical path," explained Art Morstadt, director of engineering facilities delivery. Although it would take 36 months to design and construct (the same as for a specialized plant), once the flexible plant was built, it could accommodate almost any new product without delay (other than the 2 week changeover/setup time). *Alfatine*, *Betazine*, and *Clorazine* would not get to market any sooner with the flexible plant, but subsequent new products could get to market one year earlier.

The flexible plant also offered the advantage of lower risk. If any of the three products failed in development, the plant decision was not jeopardized. The unutilized capacity could be allocated to any other new Lilly product, since it was flexible enough to accommodate almost all other processes.

Because the flexible plant offered benefits of lower risk, more time and freedom for process development and construction, and an extra year of sales on subsequent products, some people within Lilly believed that flexible plants were the ideal manufacturing strategy for the long term. "In the future, all of our plants should be more flexible," noted Morstadt.

Conclusion

Since the strategy of designing and building specialized plants had worked well in the past, Lilly had never before raised the question about what *kind* of capacity to add. Faced with a competitive new marketplace and stringent corporate goals for faster development and lower costs, many within Lilly thought that the current strategy had to change.

Steve Mueller thought over the situation. He knew many people within Lilly were attracted to the concept of flexibility, and he himself thought it offered a number of advantages. However, it was complex decision, and one that would have implications for future product launches. "This decision is bigger than just these three products. It's not a one-shot deal. We're going to have many new product launches in the future and we need to decide if flexibility is the right strategy for all of these." Since product launches were deemed critical to Eli Lilly's future, Mueller wanted to think the issue over carefully.

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[20] For each product that was transferred out of the flexible plant to a specialized facility, Lilly would incur costs of about $1 million for start-up, process validation, and source change registration with the FDA. Registration could take up to one year, so the specialized plant had to be ready in advance of starting commercial production. Process rework was not required for the transfer and process experience would not be lost.

[21] Even in the short-term, while volume for *Alfatine*, *Betazine*, and *Clorazine* were increasing, the flexible plant's excess capacity could be absorbed by making some materials for Phase III clinical trials.

Exhibit 1A Income Statement and Selected Ratios, year ending December 31 ($ in millions)

Income Statement	**1992**	**1991**	**1990**	**1989**	**1988**
Net sales	6,167	5,726	5,192	4,176	3,607
Cost of goods sold	1,897	1,654	1,523	1,256	1,125
Research and development	925	767	703	605	512
Marketing and administrative	1,624	1,536	1,426	1,150	1,020
Restructuring/special charges	566	0	0	0	0
	5,012	3,957	3,652	3,011	2,656
Operating Income	1,156	1,768	1,539	1,165	951
Other income (net)	27	111	60	165	130
Income before tax	1,182	1,879	1,599	1,330	1,081
Income tax	355	565	472	390	320
Cumulative effect of acct'g changes	-119	0	0	0	0
Net income	709	1,315	1,127	940	761
Selected Financial Ratios and Other Data					
Net income as % of sales	11.50%	23.00%	21.70%	22.50%	21.10%
R&D as % of sales	15.00%	13.40%	13.50%	14.50%	14.20%
Return on shareholders equity	14.40%	31.20%	31.20%	26.90%	24.30%
Return on assets	8.30%	17.20%	17.50%	17.00%	14.80%
Long-term debt as a % of equity	11.90%	8.00%	8.00%	7.20%	12.00%
Number of employees	32,200	30,800	29,500	27,800	26,300
Net sales per employee (000's)	$192	$186	$176	$150	$137
Net income per employee (000's)	$22	$43	$38	$34	$29
Capital expenditures	$913	$1,142	$1,007	$555	$372
Earnings per share	$2.41	$4.50	$3.90	$3.20	$2.67

Source: Eli Lilly and Company, 1992 Annual Report

Exhibit 1B Balance Sheet, year ending December 31 ($ in millions)

	1992	1991
Assets		
Current Assets		
Cash and short term equivilants	432.40	479.20
Short-term investments	295.90	303.20
Accounts receivable	898.60	834.70
Other receivables	152.50	291.30
Inventories	938.40	796.90
Prepaid expenses	288.20	234.00
Total current assets	3006.00	2939.30
Other Assets		
Investments (at cost)	242.50	276.20
Goodwill and intangibles	460.10	425.90
Sundry	892.10	874.70
Property and equipment (net)	4072.10	3782.50
Total Assets	8672.80	8298.60
Liabilities and Equity		
Current Liabilities		
Short term borrowings	591.20	690.20
Accounts payable	323.60	276.30
Employee compensation	272.80	295.10
Dividends payable	175.90	161.00
Other liabilities	575.30	410.30
Income taxes payable	459.80	439.10
Total current liabilities	2,398.60	2,272.00
Long-term debt	582.30	395.50
Deferred income taxes	169.70	415.60
Other liabilities	630.10	249.40
Shareholders' Equity		
Common stock	183.00	183.00
Additional paid-in capital	307.90	340.10
Retained earnings	4,743.10	4,693.00
Loan to ESOP	(263.90)	(286.20)
Currency adjustments	(70.20)	50.70
Less common shares in treasury	(7.80)	(14.50)
Total	8,672.80	8,298.60

Source: Eli Lilly and Company, 1992 Annual Report

Exhibit 2 Production Curve for a Specialized Manufacturing Facility

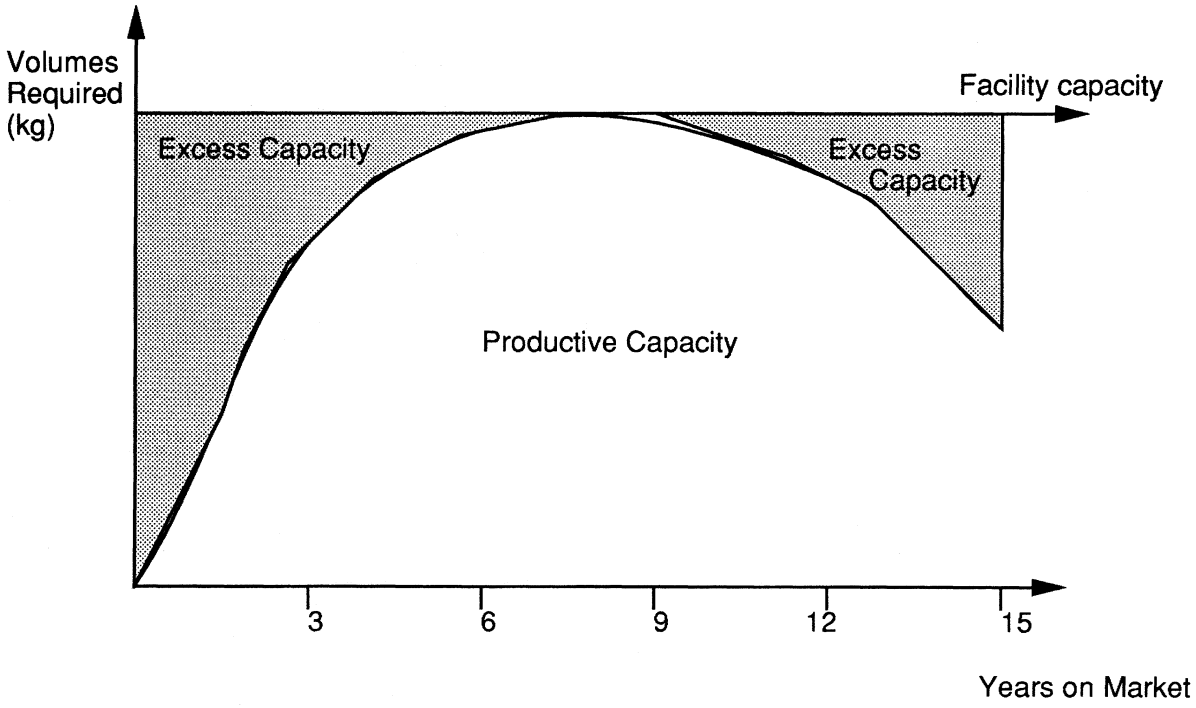

Exhibit 3 Manufacturing Facility Alternatives

OPTION 1: Specialized Facility

	Capacity in Rigs	Maximum Output in kilograms*	Construction Costs (millions)	Annual Operating Costs (millions)
Alfatine Capacity	1	16,000		
Betazine Capacity	0.25	4,000		
Clorazine Capacity	0.25	4,000		
Specialized Facility	1.5	24,000	$37.50	$6.80

OPTION 2: Flexible Facility

	Capacity in Rigs	Maximum Output in kilograms*	Construction Costs ($ millions)	Annual Operating Costs ($ millions)
Flexible Facility	3	14,625	$150.00	$9.48

* assuming average utilization (80% for specialized, 65% for flexible)

Exhibit 4 Volumes Required Annually (bulk drug in kilograms)

Volumes Required Annually (bulk drug in kilograms)

	Year 1 1996	Year 2 1997	Year 3 1998	Year 4 1999	Year 5 2000	Year 6 2001	Year 7 2002	Year 8 2003	Year 9 2004	Year 10 2005
Alfatine	7,000	8,000	9,000	10,000	16,000	16,000	16,000	16,000	16,000	16,000
Betazine	2,500	2,700	3,000	3,100	4,000	4,000	4,000	4,000	4,000	4,000
Clorazine	500	500	750	750	1,000	1,000	1,000	1,000	1,000	1,000
Total	10,000	11,200	12,750	13,850	21,000	21,000	21,000	21,000	21,000	21,000
Capacity Under Option 1 versus Option 2 (in kilograms)*										
Option 1: Specialized	24,000	24,000	24,000	24,000	24,000	24,000	24,000	24,000	24,000	24,000
Option 2: Flexible**	14,625	14,625	14,625	14,625	14,625	14,625	14,625	14,625	14,625	14,625
Excess Capacity Under Option 1 versus Option 2 (in kilograms)										
Option 1: Specialized	14,000	12,800	11,250	10,150	3,000	3,000	3,000	3,000	3,000	3,000
Option2: Flexible***	0	0	0	0	0	0	0	0	0	0

* Assumes average utilization (80% for specialized, 65% for flexible).

** Demand expected to exceed capacity in the flexible plant beginning in year 5, assuming no process yield improvements.

*** Flexible facility never has excess capacity since other products can be produced in it.

Exhibit 5 Sample Timeline for an 11-year Development Project Assuming Lilly's Current Strategy (1993)

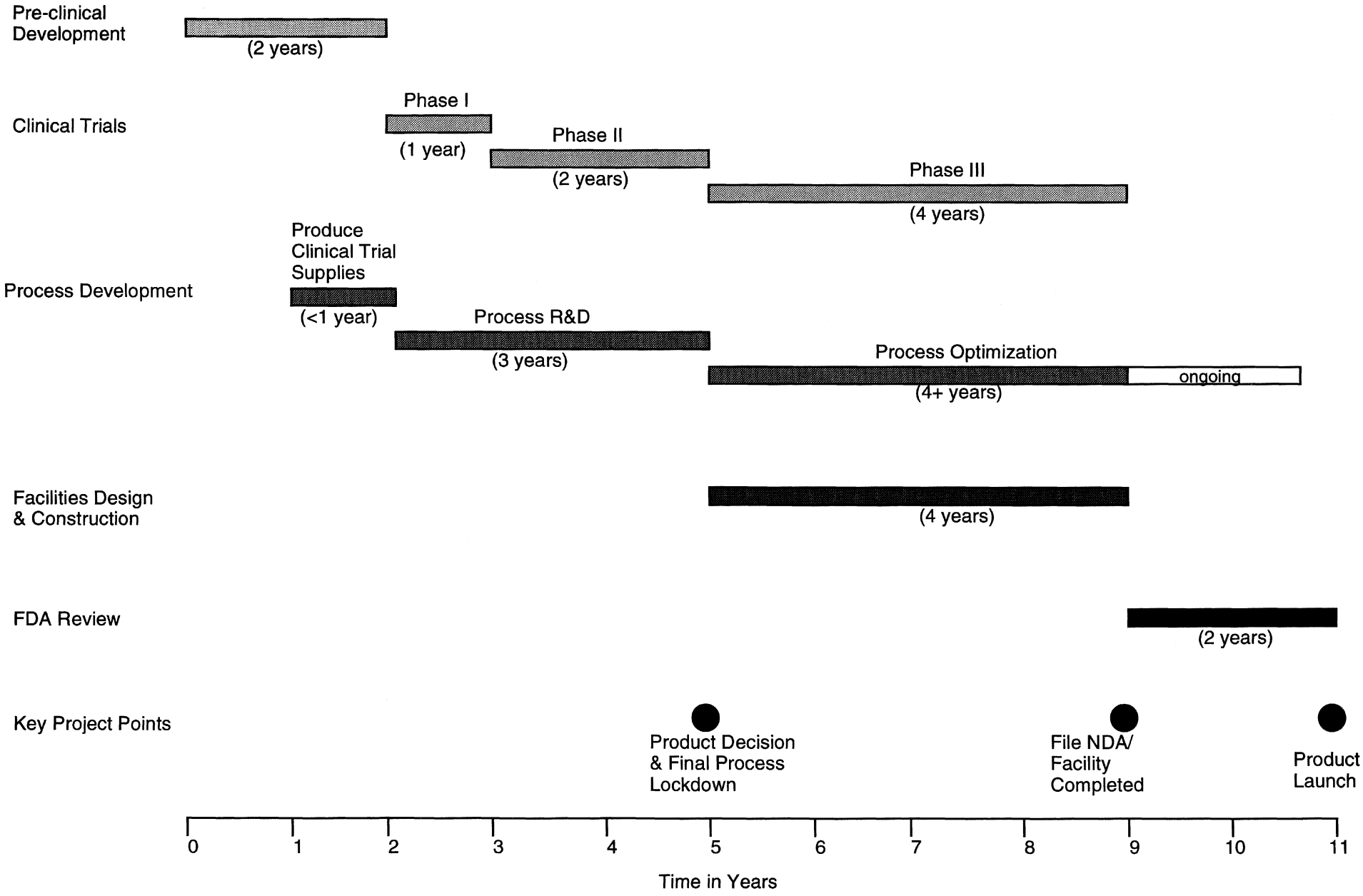

Exhibit 6 Manufacturing Capacity Requirements: Rigs Required by Product (a sample of products only)