



## Eli Lilly and Company: Innovation in Diabetes Care

"Look at these. Aren't they beautiful?" asked Larry Ellingson, Executive Director of Eli Lilly and Company's Diabetes Care Business Unit, as he showed his visitor a briefcase full of odd looking plastic devices. "They're pens -- insulin pens. All you do, " he explained as he screwed one apart, "is put a little cartridge of insulin in here; close it up like this; turn this dial to the amount of insulin you need; poke the needle just under your skin (which he *didn't* demonstrate); and squeeze this trigger. That's all there is to it. Then you just put this cap over the needle and put it back in your briefcase, purse, or pocket until your next meal, when you take a shot again. The patients will just love it."

If history was any guide, Ellingson was right: they *would* love it. Lilly's principal competitor in the worldwide insulin business, Denmark-based Novo Nordisk, had introduced insulin pens to the European market several years earlier with great success. Pens were a more convenient way for patients to take insulin. Conventionally, patients carried a separate syringe, inserted its needle into an insulin vial, pulled its plunger out to draw slightly more than the desired amount of insulin into the syringe, flicked the syringe while holding its needle up to dislodge any air bubbles that clung to the walls of the syringe's cylinder, and then squeezed the plunger slightly to force those bubbles -- and some insulin -- out of the syringe. Only then could they inject themselves with insulin. This process typically took more than a minute, whereas patients could prepare and administer a pen injection in as little as 10 seconds.

It was early in 1995, and Novo was building a new plant in the United States to produce insulin cartridges for its pens. Ellingson hoped that Lilly's new line of pens (**see Exhibit 1**), the result of a multi-million dollar investment, would blunt the advantage Novo had enjoyed with convenience-conscious customers and stabilize Lilly's share of the worldwide insulin market.

Insulin was an important product for Lilly, one of the world's largest pharmaceutical manufacturers with sales of over \$5 billion (see Exhibit 2). Insulin in fact was Lilly's second largest revenue producer after its widely prescribed drug for depression, Prozac.

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*Professor Clayton M. Christensen prepared this case as the basis for class discussion rather than to illustrate either effective or ineffective handling of an administrative situation. The data in this case have been disguised to protect the proprietary interests of the company.*

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## Diabetes and Insulin

Diabetes is actually two fundamentally different diseases that share a similar set of symptoms: Type I patients produce no insulin, the hormone necessary for cells to utilize glucose, while Type II patients cannot efficiently use the insulin their bodies produce. Type I, also known as juvenile diabetes, usually begins during childhood or puberty. Type II, known as adult-onset diabetes, is manifest later in life (usually after the age of 40) and usually is associated with -- and possibly caused by -- obesity. Digestive processes convert most food into glucose (a simple sugar) and then pass that glucose into the blood as the body's main source of energy. Body cells are able to burn or metabolize glucose, however, only when there is insulin present, acting as a sort of catalyst for "burning" the glucose. Because they either cannot produce insulin in the pancreas (Type I) or use the insulin they produce (Type II), those with diabetes (hereafter simply called "patients") can have high concentrations of unmetabolizable glucose in their bloodstream.

Patients need to inject the precise amount of insulin required to metabolize the glucose produced by their digestive system. If they inject too little, the resultant high blood-sugar levels cause a slow deterioration of the body, particularly of the eyes and kidneys. Low blood-sugar levels caused by an overdose of insulin, though, can rapidly precipitate unconsciousness and, potentially, death.

Many Type II patients can treat their condition with oral medications that either cause their pancreases to produce more insulin or enhance the sensitivity of their body tissues to the insulin they naturally produce. Some Type II and all Type I patients, however, must take daily injections of insulin to survive. Insulin cannot be taken orally because it is a protein and would be broken down by the digestive system.

All Type I patients must begin insulin injections immediately upon diagnosis. Most Type II patients, however, progress through several stages. Typically, their diabetes initially is so mild (they can use most of the insulin they produce) that they aren't symptomatic<sup>1</sup> -- their illness remains undiagnosed until it is discovered during a routine physical exam or in the course of treatment for some other disease. Upon initial diagnosis, many can reduce their levels of blood glucose to normal through a combination of diet, exercise and weight loss. Many Type II patients subsequently reach a point, however, when they require oral medications. As the disease progresses the oral agents often fail. At that point, Type II patients join the Type I's in having to take insulin injections.

In 1995 Europe and North America accounted for over 80% of the world insulin market because the rates of diagnosis in those regions were high relative to other areas; because the incidence of obesity was higher; and because a larger proportion of Type II patients tended to be treated with insulin. Approximately 2% of the world population had diabetes, although many remained undiagnosed with Type II diabetes. Of the diagnosed diabetic population, 10 percent were Type I (this population was increasing by 2 to 3 percent a year) and 90 percent were Type II (increasing at 4 to 5 percent a year).

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<sup>1</sup> Three symptoms typically induce a patient with diabetes to seek medical attention: 1) A rapid loss of weight, caused by their inability to metabolize the food they eat (those with diabetes quite literally are starving at this stage, even though they eat larger-than-normal amounts of food). 2) Constant thirst, and abnormally high frequency and amount of urination. This happens because the body's rate of urination is driven not only by how much water is in the body, but by how much glucose the kidneys secrete. Hence, the body dehydrates. 3) Blurry vision, caused by the osmotic effects of high levels of glucose in the eye on the lens of the eye.

## Early Discovery and Development of Insulin

Until 1921 there was no effective treatment for diabetes. Type I patients could expect to live approximately one year from the time of diagnosis. Primary treatment was a starvation diet, based upon the theory that less food generated less blood glucose and, therefore, prolonged life -- slightly. Diabetes wards in hospitals were populated by emaciated bodies, dying from a combination of untreated diabetes and malnutrition. The physical appearance of patients in diabetes wards was later likened to that of prisoners in the Nazi concentration camps of World War II.

In 1921, four researchers from the University of Toronto, F. G. Banting, J. J. R. MacLeod, C. H. Best, and J. B. Collip, had begun experimenting on dogs with pancreatic extractions of insulin. By 1922, these researchers were injecting insulin extracted from animals into human patients with miraculous results. Patients with diabetes could finally metabolize their food. Those who watched their nearly instant recovery from starvation likened what they saw to the resurrection of the dead (Exhibit 3). Banting and Best received the 1923 Nobel prize for this work.

The researchers from Toronto needed capital to begin consistent production in large quantities and offered the Indianapolis-based drug maker, Eli Lilly and Company, an exclusive license to produce and sell insulin in the United States. Lilly immediately began commercial development of the product, and by the fall of 1923 25,000 Americans were receiving insulin Lilly extracted from pancreases of cows and pigs. Half of all Eli Lilly's profits soon were derived from insulin sales. A number of other companies subsequently began producing insulin in other regions of the world. These included two Scandinavian companies, Nordisk and Novo, and the German chemical giant, Hoechst. By 1995, Lilly and Novo-Nordisk (the two companies merged in 1989) dominated the world market. Hoechst had a significant market position only in Germany.<sup>2</sup> The sizes of the world insulin market by region and the major competitors' market shares, are detailed in Exhibit 4.

## Subsequent Improvements in Insulin

Over the next sixty years, Lilly and its competitors improved their insulins along two dimensions. The first was its purity. The second was in its "time profile"-- matching the rate at which injected insulin was absorbed into the blood<sup>3</sup> with the rate at which glucose was absorbed into the bloodstream.

### Purity and the Development of Humulin

Parts per million (ppm) of proinsulin, the impurity which caused the majority of side effects from insulin therapy, dropped from 50,000 ppm in 1921, to 10,000 ppm in 1970, and 10 ppm in 1980. Still, though, all insulin products were derived from the pancreases of either cows or pigs (pork insulin was closer in its molecular structure to human insulin than was beef-derived insulin). While similar to that of humans, animal-derived insulin could never be molecularly equivalent to

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<sup>2</sup> In 1995 there were also a few small producers of insulin in economically less developed countries as well. Because their process technology for extracting insulin from animal pancreases was not sophisticated, many of their insulins were notoriously impure.

<sup>3</sup> Patients had to be careful to inject insulin into subcutaneous tissue (under the skin) and *not* directly into the bloodstream. Doing so would suddenly lower blood sugar, precipitating unconsciousness, brain damage, and possibly death.

human insulin. A fraction of a percent of the population with diabetes became resistant to insulin as a result.

In addition to this problem with animal insulins, Lilly feared an insulin shortage caused by a combination of decreased red meat consumption and increased insulin usage. In response to these concerns, Eli Lilly teamed with the biotechnology company Genentech to genetically engineer bacteria that could synthesize and secrete human insulin. The result of this effort, branded in 1980 as Humulin,<sup>®</sup> represented the supreme breakthrough in insulin product and process technology -- a 100% pure insulin that was structurally identical to the insulin healthy humans produced. Lilly invested over \$700 million to build the first large-scale biotechnology plant in the world to produce its Humulin.<sup>®4</sup> The market responded poorly to Humulin<sup>®</sup>, though. Consumers resisted its premium price and retailers were reluctant to add yet another set of SKUs to their already crowded refrigerators of insulin products. The substitution of Humulin<sup>®</sup> for animal insulins occurred at a slow pace, as a result, and it was not until the early 1990s that Humulin<sup>®</sup> accounted for 80% of Lilly's insulin volume. "In some developing countries the animal insulins they make have all sorts of impurities in them," noted Kathy Wishner, one of Lilly's senior medical executives. "But all markets are getting more sophisticated. Levels of impurities that were accepted a generation ago would not be tolerated today. "Nonetheless," added researcher Bruce Frank, "In retrospect the market was not all that dissatisfied with highly purified pork insulin."

The market's sluggish response to Humulin<sup>®</sup>, its cost, and Lilly's high share of the North American insulin market (which often exceeded 85% and made it difficult to generate additional volume through a new product such as Humulin<sup>®</sup>), all contributed to decreasing support for continued investment in the insulin business at Lilly. Ron Chance, another Lilly researcher, recalled, "At that point in time people were saying, 'We can't get any better than Humulin<sup>®</sup>. And we can't grow the business. It's time to do something else.' As a result, many of us went to other projects, like the human growth hormone."

Through the 1980s, particularly after Novo Nordisk introduced its version of bio-engineered human insulin in 1984, insulin became viewed essentially as a commodity product -- the products of Lilly, Novo and Hoechst were essentially identical in purity and efficacy. Nonetheless, because of the high cost of clinical trials for new bio-technology products and the cost of an efficient manufacturing facility, entry to the industry was limited, and as of 1995 the industry had not been afflicted by the sorts of price battles that characterize the markets for many commodity products.

#### Action Profile

Glucose flows into the blood as food is digested. This flow rate, if graphed, resembles a bell-shaped curve which reaches its peak flow rate about 1.5 hours after a meal. Some glucose is taken into the liver, converted into a substance called *glycogen*, and stored there. To provide the body with between-meal energy, the liver converts this stored glycogen back into glucose and secretes it at a steady rate back into the bloodstream.

In non-diabetic persons, the body senses the amount of glucose flowing into the blood from these two sources and signals the pancreas to secrete an offsetting amount of insulin to maintain about 100 milligrams of glucose per deciliter of blood. To achieve the same level of control over

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<sup>4</sup> The pharmaceutical industry's cost of developing a new drug, and of managing its progress through clinical trials to receive regulatory approval, averaged over \$300 million per approved drug in 1995.

blood sugar (and thereby avoid the complications of excessive or insufficient blood glucose), patients with diabetes needed insulins that are absorbed from the subcutaneous injection site at two different rates -- one to be absorbed into the blood at a slow, constant rate, to offset the flow of glucose from the liver, and the other to be absorbed into the blood at a faster, bell-shaped pace, to offset the flow of glucose from digestion. Hence, many patients mixed a regular-acting and slow-acting insulin together in their syringes for most injections. These rates of flow are depicted in Exhibit 5.

Because of these different flow patterns, patients who wanted to control their blood glucose levels carefully had to take injections of regular insulin before every meal. Unfortunately, many found injections to be inconvenient or uncomfortable, and took only one or two daily injections of long-acting insulin.<sup>5</sup> The resultant unhealthy pattern of insulin and glucose flows in the bloodstream of these patients gave them high levels of blood glucose in the morning and low levels in the afternoon -- causing a high incidence of near-term emergencies and long-term complications.

Unfortunately for the small proportion of patients taking pre-meal shots to keep better glucose control, the fastest-acting available insulins followed a flow or action profile that was slightly slower than the rate of glucose flow from digestion, as depicted in Exhibit 5.<sup>6</sup> They therefore suffered a temporary high level of blood glucose after meals unless they took their injection about 40 minutes prior to eating. For most patients, however, taking an injection 40 minutes prior to each meal was risky and inconvenient. For example, a diabetic could take an injection just prior to leaving work in the evening, planning to drive home and start eating dinner an hour later. If caught in a long traffic jam, however, the result could be disastrous. Similarly, if a diabetic took an advance injection prior to eating out, but then was unable to eat the type or amount of food he or she had planned upon in the injection, high or low blood glucose could result. Hence, many of even the most careful patients simply injected themselves just before their meals, and lived with the mismatch in flow rates.

To respond to this problem, in the late 1980s Lilly launched an effort to develop an insulin that could mimic more closely the normal physiologic secretion of insulin in people without diabetes. The result, code-named *Match*, was successful. By 1994 it was clear that *Match* was absorbed into the blood after injection at a rate that was much closer to the rate at which glucose was absorbed into the blood after a meal. Consequently, patients using *Match* insulin in the clinical trials required for regulatory approval were able to achieve better control of blood glucose levels after meals, reporting fewer incidents of high and low blood glucose, compared to patients using regular insulin.

By the end of 1995, *Match* had been approved for general use by two governments. In addition to launching Lilly's new line of pens successfully, launching *Match* in each major market in 1996 was high on Larry Ellingson's innovation agenda. Novo Nordisk's own version of fast-acting insulin, whose action profile reportedly was similar to *Match*, was two years behind Lilly in the regulatory approval pipeline.

Exactly how Lilly should market *Match* was proving to be a vexing question for Ellingson's team. In the United States where Lilly's share of the insulin market hovered near 80% in 1995, and it appeared that every vial of *Match* that Lilly sold to an existing customer would directly supplant a vial of regular insulin which that customer had been purchasing. In Europe and Japan,

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<sup>5</sup> Experts believed that only 20% of insulin-injecting patients actually took a shot before each meal.

<sup>6</sup> Regular-acting human insulin existed chemically as a hexamer in its vials. Once it was injected into subcutaneous tissue it had to dissociate into dimers and monomers before it could be absorbed into the blood. This dissociation normally took 30-45 minutes, and was the reason why regular-acting insulin had to be injected 40 minutes prior to meals, in order to match the rate of flow of glucose into the blood.

where Lilly's and Novo's market share positions essentially were reversed, there was greater immediate-term potential for Lilly to win new customers with *Match*. Remembering Lilly's struggles to achieve premium pricing for Humulin®, Ellingson was also concerned that *Match* be capable of sustaining a premium price relative to regular insulin, given its better performance.

In addition to its fast-acting *Match* insulin, Lilly researchers had been working on a new, long-acting "basal" insulin with a flatter action profile than that of the available insulins depicted in Exhibit 5. Intended to provide a closer fit to the level pattern of glucose released into the bloodstream by the liver, this program had reached the point where significantly more money would need to be committed to it, in order to advance it to the next phase of development.

### Lilly's Organizational Structure

Historically, like most pharmaceutical companies Lilly had grown opportunistically. The way the human body worked: -- issues such as how and why disorders arose, and how and why the body healed itself, were poorly understood. It was therefore difficult to predict, when researchers developed a new chemical compound, which if any disorders of the body that compound might address. Hence, drug companies often got into the business of treating particular disorders by serendipity. As the mechanisms of action of diseases and of particular classes of molecules on various body functions became better understood, it had become increasingly possible for scientists to deliberately set out to develop a drug for a particular disorder. But even in 1995, random success continued to play an important role in the fortunes of pharmaceutical companies.

To manage this mechanism of growth, Lilly, like most pharmaceutical companies, had adopted a functional organization. Lilly Research Laboratories was responsible for the discovery of all new compounds. Lilly's medical division was responsible for the design and management of the clinical trials required to gain regulatory approval for each new drug. Its development group developed the formulations -- liquids, tablets, injectables -- for each new drug. Its manufacturing organization was responsible for manufacturing all drugs; market research handled market analyses for all diseases; and so on.

Although the company's single marketing organization had long had a similar responsibility for marketing all of the company's products, it had been reorganized in 1994 into three "global business units" -- Endocrine, Central Nervous System, and Internal Medicine -- to create better focus on specific diseases in which Lilly had important drugs. Under the Endocrine umbrella was the Diabetes Care Business Unit, headed by Larry Ellingson, which had responsibility for over-all marketing and planning for all diabetes-related products.

In addition to this organizational structure at the corporate level, responsibility for marketing, distribution and sales for all Lilly products was vested in its "affiliates" -- companies organized within each country in which Lilly had a significant position. Hence, the corporation provided products to its U.S. affiliate, which marketed them in the United States; to its Italian affiliate, which marketed them in Italy; and so on.

Lilly's financial and accounting systems were aligned with these functional and affiliate structures. Hence, it was relatively easy to learn what the corporation's total manufacturing, selling or research costs were; or what the profit made by its German affiliate was. But it was very difficult to determine accurately the fully-costed profitability of specific product lines -- even products as significant as insulin.

All commitments of resources the corporation made to new products under development -- novel insulins and pens were examples -- were made by two corporate-level committees, which reviewed proposals to initiate new developments or fund their progress to further stages in the development pipeline.

Like most pharmaceutical companies, Lilly's salesforce, which represented the entire Lilly line of drugs, did much of its selling through "detailing" -- having salespeople call on physicians in their offices to explain the advantages of their drugs, and to persuade them to prescribe their company's drugs over those of competitors. As drug manufacturers' product lines proliferated and doctors' schedules became more crowded, detailing was proving to be an increasingly difficult vehicle for communicating the benefits of new drugs. Increasingly, governmental health ministries in Europe and managed healthcare organizations in the U.S. were taking more authority to choose which drugs their physicians could and could not prescribe. In particular, where two or more essentially identical products were available in the market -- as was the case with regular and long-acting insulin -- the largest and most powerful of these institutions were applying strong pressures on drug manufacturers to reduce their prices.

### Problems in The Treatment of Diabetes

Lilly planners mapped diseases along the two spectra shown in Exhibit 6. The first was their duration. *Acute* diseases were short term in character while *chronic* diseases persisted for years -- and in the case of diabetes, for a lifetime. The second dimension of differentiation measured the degree of behavioral change in the patient required to effectively treat the disease. Hence, bacterial infections were acute diseases that required little behavioral change; patients generally had only to receive injections or take pills of drugs such as Lilly's highly potent antibiotic, Ceclor.<sup>®</sup> Depression was classed as a chronic disorder, and its treatment also required little behavioral change on the patient's part. For many patients suffering from depression, taking Lilly's Prozac<sup>®</sup> on a daily basis was sufficient to allow them to lead happy, normal lives.

Effective treatment of diabetes, however, required extensive behavioral change by patients. In addition to multiple daily injections of insulin, patients needed to monitor their blood glucose levels several times daily by pricking a finger; to carefully control the amount and type of food they ate; and to exercise in a regular and consistent way. Careful weight control was particularly important.<sup>7</sup>

The right-side vertical axis in Exhibit 6 depicts Lilly managers' assessment of who most strongly determined the nature and extent of care in various diseases. They felt that for diseases toward the bottom of the map, physicians were the primary determiners of therapy--they prescribed the pills. For chronic diseases requiring behavioral modification, however, the patient effectively determined the nature and extent of his or her therapy. Healthcare professionals could recommend what the patient should do, but whether the patient followed their advice was at his or her discretion. Some patients--about 10% of the total diagnosed population--actively embraced every element of state-of-the-art therapy and lived free of the complications of diabetes such as blindness, kidney failure, and neuropathy for their entire lives. Most, however, tended to be sloppy in managing their treatment -- by eating inappropriately, not taking insulin injections when they ate, not exercising, remaining overweight, and so on. Exhibit 7 describes the proportion of patients who followed various treatment regimens.

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<sup>7</sup> Diabetes could actually disappear in many obese Type II patients, in fact, if they reduced and maintained their body weight to normal levels.

The tendency of most patients not to follow therapies that were known to pre-empt long term complications mirrored the patterns of postponement and denial that were typical amongst smokers, many of the overweight, and those with cardiovascular disease. The cost to society of this behavior was enormous. While the cost of health care for the average person in the United States was about \$2,600 per year, the average cost per diabetic patient exceeded \$10,000 per year. Of this incremental cost, about \$220 was spent for insulin, \$125 for syringes, and \$300 for blood glucose testing equipment and supplies. The remainder was for doctors' office visits, other testing, and most importantly, the treatment of complications such as blindness, kidney failure, cardiovascular disease, and loss of blood circulation in the extremities.

Because of the prominent role patients played in determining the regimen they followed, Ellingson and his colleagues increasingly were viewing success in the diabetes care business as an issue of effective consumer marketing, rather than it being a traditional pharmaceutical business.

## The Industry's Innovative Response

Beginning in about 1980, the diabetes care industry began a stepped-up technological response to the problem of most patients' non-conformance to regimens that were known to pre-empt complications and prolong their lives. The most important of these innovations were the development of lightweight, portable blood glucose meters; the use of information technology to enhance and make more convenient the interaction between physicians and patients; the development of insulin pens, and establishment of diabetes education centers.

### Portable Blood Glucose Meters

Historically, the only way patients could test their level of blood glucose was by dipping a strip of chemical-coated paper into a urine sample, in a litmus paper-like test for the presence of glucose. This was a crude, indirect measure of blood glucose level, because once that level exceeded a threshold of about 175 mg/dl, the kidneys began to remove glucose from the blood and excrete it in the urine. While glucose in urine was useful information to patients, it was a *lagging* indicator of *blood* glucose -- it reflected a situation several hours old, and it detected high, but not low blood sugar. There was no available method to detect the onset of low blood sugar before it reached the perilously low levels at which patients became symptomatic. Because of this, even those patients who proactively worked to control their blood glucose levels would keep their level above normal, in order to minimize the chance of a severe insulin reaction with the unconsciousness it could bring. The technology to measure actual blood glucose levels existed, but the equipment was large and expensive, and tests could only be done in hospital laboratories. Eli Lilly was the dominant maker of urine glucose testing products. Its Testape® brand product, in fact, had enjoyed a market share of over 90% throughout the 1960s and 1970s, netting about \$20 million in revenues to Lilly per year at its peak in the early 1980s. The advent of home blood glucose monitoring had subsequently eroded the market for urine testing products significantly.

In 1980 the Ames division of Miles Laboratories developed a portable blood glucose meter about the size of a paperback book. Patients using it would prick their finger and place a large drop of blood on a chemical reagent strip. The reagent would turn colors, depending on the amount of glucose in the blood. The meter would then reflect a light off the colored strip; measure the depth of its color; and then translate that color into a relatively accurate ( $\pm 10\%$ ) estimate of blood glucose level. The reagent strips could be used only once. This technology made a huge difference in the lives of those patients who assertively wanted to keep their blood glucose levels near normal.



It gave an accurate reading of the patient's *current* condition, and measured low as well as high levels. Portable blood glucose meters could be used at home, at work or in the car. And the test took less than a minute, any time of the day or night -- a vast improvement in convenience over having to visit a hospital or doctor's office laboratory.

Patients using the meters quickly found them to be liberating. When they measured excess glucose, they could inject insulin to bring it down. When they measured low glucose they could eat carbohydrates to raise it. And most importantly, with tighter feedback loops between what they ate, how much insulin they injected, and their resultant level of blood glucose, patients developed personalized algorithms for how much insulin they needed to offset different types and amounts of food they ate. This gave them much more freedom in choosing what and when they would eat, as long as they compensated in advance for what they would eat by injecting the right amount of insulin.

Within two years, Ames had been joined by at least seven other companies in making meters and their reagent strips. Each company's strips could only be used in its meters, and they tended to price these products like razors and blades -- nearly giving away the meters in order to build volume and make money selling strips. Out of this group of companies, three had come to dominate the blood glucose testing market by 1990: the Lifescan division of Johnson & Johnson; the Ames division of Miles Laboratories; and Boehringer Mannheim, a German manufacturer. Seeking to leverage its brand name in diabetes care, Eli Lilly's diagnostic equipment division had developed and advertised a meter in 1985 that measured glucose without needing expensive single-use strips, but the meters proved unreliable and had to be withdrawn from the market.

As Exhibit 8 shows, by 1995 the market for blood glucose meters and strips had grown to \$1.5 billion, roughly equalling the size of the world insulin market. Nearly 80% of Type 1 patients owned meters, while less than 30% of Type II patients owned them. The rate of technological change in meters was also brisk, as the manufacturers sought to offer meters that were lighter, less complicated, and faster. As a result, in 1995, nearly 90% of all meters in use were less than two years old. Industry analysts predicted that within the next decade, meters would be developed that could measure blood glucose through the skin without requiring patients to prick a finger for a blood sample.

In addition to these blood glucose readings, which provided single-point-in-time measures, physicians were increasingly administering another test, HbA<sub>1c</sub>,<sup>8</sup> as a useful measure of a patient's longer-term level of blood glucose control. This test, which was recommended to be done quarterly, measured the proportion of hemoglobin cells in the blood to which glucose molecules were bonded. The higher a patient's average blood glucose levels were, the higher this proportion would be. In 1995 the HbA<sub>1c</sub> test was still relatively expensive to administer and was typically performed on blood samples taken in doctors' offices and analyzed in independent laboratories. As a result, only a small proportion of patients took HbA<sub>1c</sub> tests quarterly.

## Information Technology

Industry visionaries saw great potential in marrying data generated by these tests with advances in telecommunications and computing technologies. For example, data from blood glucose tests could be stored in meters and periodically downloaded through home computer modems to a computer in the physician's office. Algorithms in the physician's computer might then analyze the data to assess the patient's over-all level and pattern of blood glucose control; compare it to a larger patient population to express probabilities of various complications occurring if that level of

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<sup>8</sup> The formal name of this test was the glycosylated haemoglobin test.

control were to persist; and recommend adjustments in the patient's treatment regimen. Doctors could then discuss their findings and recommendations through televideo, thus eliminating the inconvenience and expense of office visits.

## **Insulin Pens**

The second wave of innovation targeted at making diabetes care more palatable to patients was Novo's development of insulin pens, beginning in 1985. As explained in the opening paragraphs of this case, pens offered patients a faster, more convenient way to inject insulin. Novo had marketed its pens aggressively in Europe with impressive financial results. Insulin packaged in pen cartridges garnered a 30% price premium over insulin in vials. Furthermore, the added convenience seemed to have stimulated demand for insulin -- European pen users were much more likely to take multiple daily injections, rather than a single daily injection of time release insulin that was common to most users of conventional syringes and vials. Studies had shown that the average patient increased his or her insulin consumption by about 20% when shifting to multiple daily injections. Novo's innovative pens drove significant increases in its profits, revenues, and European market share through the 1980s (see Exhibit 9). Analysts estimated, in fact, that insulin in pens had grown to account for over one-third of Novo's total insulin sales by 1995.

Since introducing its first NovoPen I in Europe in 1985, Novo had followed with a succession of improved versions: the NovoPen II in 1987 and the NovoPen III in 1990. Pens proved highly popular in the Japanese market as well, particularly among Type II patients. In response, Novo introduced a small-capacity 1.5 ml pen in 1992 for physically smaller Asian adults and European juvenile patients. In addition, Novo introduced its first of a line of disposable, pre-filled pens in 1991.

Novo had made a half-hearted and unsuccessful attempt to market pens in North America in the late 1980s. Whereas a large proportion of European patients had already been converted to a therapy of multiple daily injections, most American patients took one injection daily. And Novo did not have the salesforce coverage needed in North America to convince such patients and their physicians that the convenience of pens was worth their premium price. By 1995, however, it appeared Novo was mounting a serious pen-based assault on North America: it had begun constructing a large plant in North Carolina to make insulin cartridges for its pens.

Lilly had introduced a pen in Europe in 1991, but as of 1995 still had not launched it in the U.S. market -- though it planned to do so in 1996. "It just didn't make sense for us to bring it to market earlier," a Lilly executive stated. "Because we have such a large share of this market, we'd only have cannibalized our own sales of insulin in vials with the pen cartridges. And quite frankly, the gross margin on the vials is better than the margins we think we'll get from cartridges."

## **Controlled Diabetes Services**

Although the convenience of meters and pens had been a boon to patients who already were somewhat disposed to manage their disease carefully, the fact that most patients persisted in sloppy self management remained a festering issue. European and North American governments, insurers, managed care providers (health maintenance organizations) and employers were all eager to find a solution to the high and escalating cost of treating the complications of diabetes as part of their larger efforts to control escalating health care costs.

"The real issue," reflected Mitch Tull, a Lilly product planning manager, "Is that while everyone wants a solution to the cost of diabetes care, nobody finds it in their interest to invest in long-term patient behavior modification to help them avoid costly complications. Take managed care, for instance. The average member of a health maintenance organization belongs to an HMO only for 2 or 3 years. People keep switching health care plans because they change jobs, their employer changes plans, or they switch to another of several plans their employer offers. So why should an HMO spend any money trying to prevent the complications of diabetes today when the odds are that the patient will belong to some other plan when the complications finally occur 10 to 15 years from now?"

"In fact," Tull continued, "Most people's really expensive complications occur when they're on Medicare (in the United States). You'd think that the governments in the U.S. and Europe would be willing to invest in programs to change the behavior of those with diabetes, but they're short-term focused too. The near term budget pressures everywhere are too great -- and the savings won't really begin to materialize for 8, 10, or maybe even 15 years, from any innovations that help patients achieve better control. It's frustrating. You've got this huge chunk of cost out there. Somebody ought to be able to make money helping everyone save money. But none of the major players seems to have a long enough payback horizon." That's why we set up Controlled Diabetes Services (CDS)."

CDS was established by Lilly in 1994 as an outlet where patients could get the information, educational materials, diet management aids, blood glucose test equipment, and syringes they needed to manage their disease. CDS centers were staffed with diabetes nurse-educators -- professionals who had specialized training in total disease management for diabetes. Any patient could visit a CDS outlet and leave with a total management regimen, including a dietary plan, daily exercise routine, and a system for testing blood glucose and taking insulin or oral agents that was tailored to the patient's own needs and lifestyle.

Lilly hoped CDS would make money from retailing diabetes care products other companies manufactured (such as blood glucose meters), and from education and training fees Lilly hoped to win from insurers, managed care providers, and employers.<sup>9</sup> CDS's value proposition, essentially, was that it could provide motivation and education for the patient-subscribers of large managed care organizations more cost-effectively than could the organizations themselves. For this reason, as many of the centers as possible were located in strip malls in high-traffic areas, as close as possible to large health maintenance centers in 12 United States cities. Related concepts were being implemented in Canada, the Netherlands, and other countries.

Lilly projected revenues of about \$1,300 per patient in the CDS system, anticipating the 5% to 15% profit margins that were typical for the sorts of activities in which CDS engaged. The CDS initiative was the Diabetes Care Business Unit's strategy of implementing Lilly Chairman Randall Tobias' vision that Lilly could no longer be just a drug company--but needed to provide value-added total solutions or improvements in bottom-line outcomes, for the disease states in which Lilly provided products and services.

## The Management Challenge

"You know, even though the pharmaceutical industry spends an enormous amount of money on innovation," Larry Ellingson reflected, "The *pace* of innovation isn't usually that frenetic.

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<sup>9</sup> The CDS centers were explicitly set up to serve as education centers, and therefore did not sell products typically sold by registered pharmacists, such as insulin and oral agents.

Because of the regulatory approval process and differences in habits and regulations across countries, companies like ours typically have to approach important innovations at a pretty measured, thorough pace. But when you look at everything going on here -- launching our pens *and* our *Match* insulin in most of the world's major markets in 1996; figuring out what all this test data and information technology means for Lilly; managing CDS so that we learn how to make money selling education services; and still being sure we have adequate resources devoted to the new products in our development pipeline -- this is *a lot* for an organization like ours to tackle. And beyond these things there is another list of initiatives we haven't even talked about yet -- like product line rationalization and working on our supply chain. We feel over-worked now, but believe me, it will get worse before it gets better.

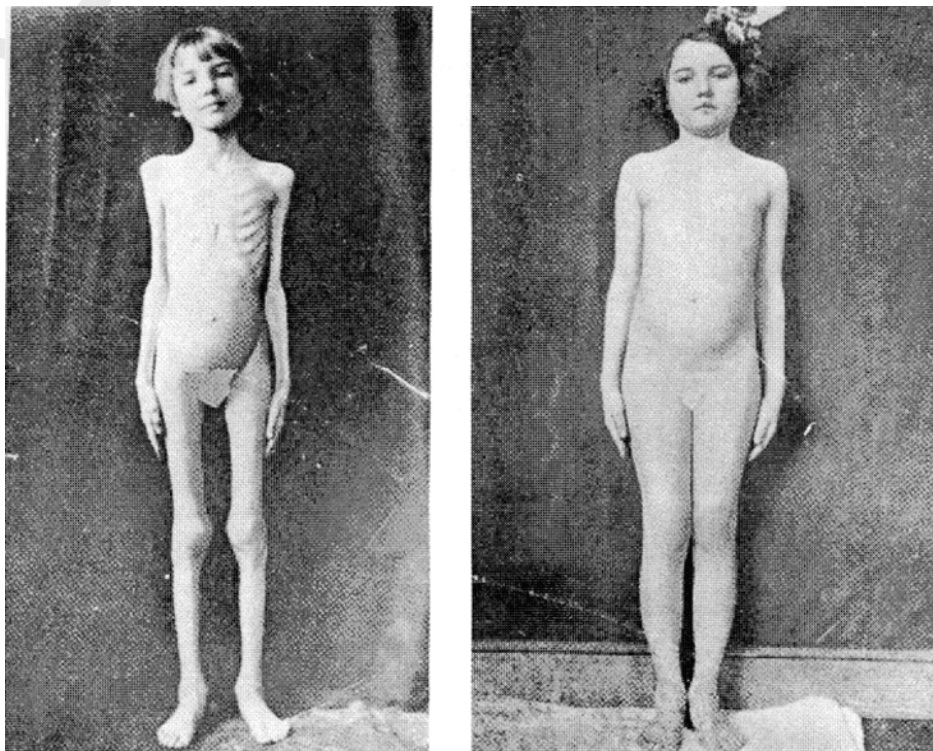
"We clearly need to prioritize these things, but frankly, they're all important -- every one of them can have significant long-term *and* near-term impact. It's one of the unique challenges of living in this world of intense competition, technological change and long development and approval lead times -- you can't plan very well when it's all going to happen. And when these things are through the pipeline and ready to be launched, like they are for us right now, you've got to do it just as fast and as effectively as you can."

**Exhibit 1:** Lilly's Insulin Pens, Slated for Market Introduction in 1996**Exhibit 2:** Summary Financial History: Eli Lilly and Company, selected years, 1987-1994

	1994	1993	1992	1990	1987
Net Sales	\$5712	\$6452	\$6167	\$5192	\$3236
Cost of Sales	1680	1959	1897	1586	1087
<b>Gross Margin %</b>	<b>71%</b>	<b>70%</b>	<b>69%</b>	<b>69%</b>	<b>66%</b>
Research & Development	839	954	925	702	434
<b>R&amp;D as % of Sales</b>	<b>14.7%</b>	<b>14.8%</b>	<b>15%</b>	<b>13.5%</b>	<b>13.4%</b>
Other costs	1494	2838	2163	1305	1136
Profit after taxes	1286	480	709	1127	643

Source: Annual Reports of Eli Lilly and Company

**Exhibit 3:** The miracle of insulin, manifest in a diabetic child, 1922. The left-side photograph was taken just prior to the start of insulin injections; the right photo was taken three months later.



Source: Bliss, Michael, *The Discovery of Insulin*. Chicago: The University of Chicago Press, 1982, p. 129. Used with permission.

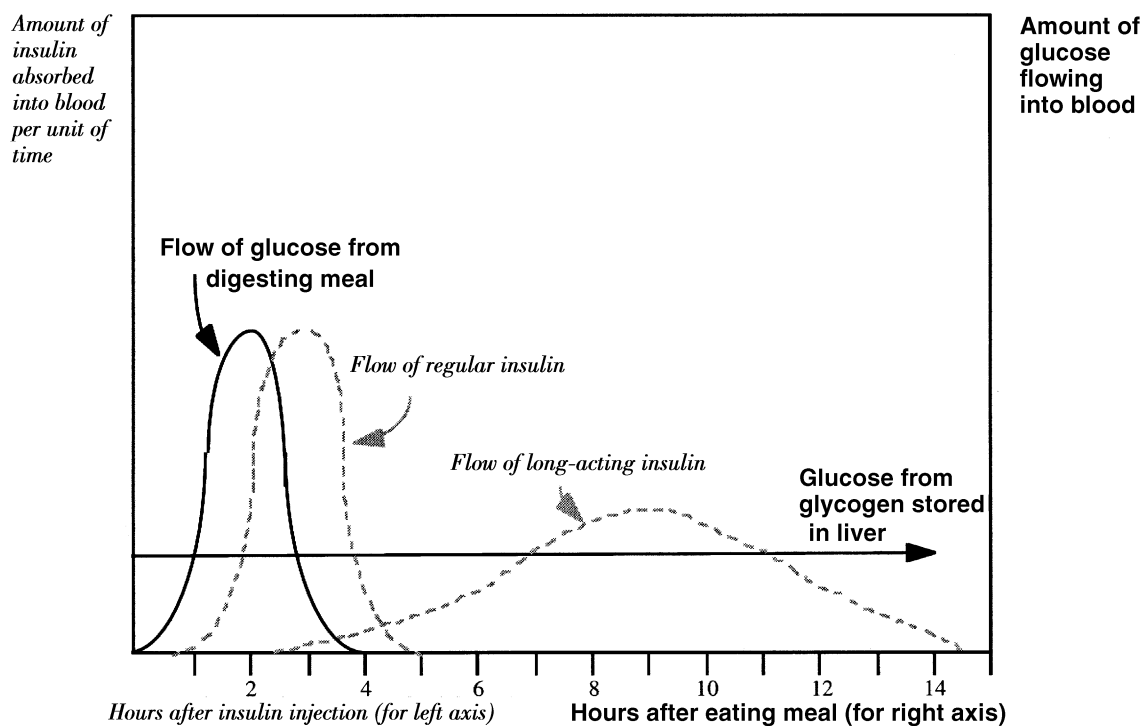
**Exhibit 4:** Competitors' Shares of Major Insulin Markets

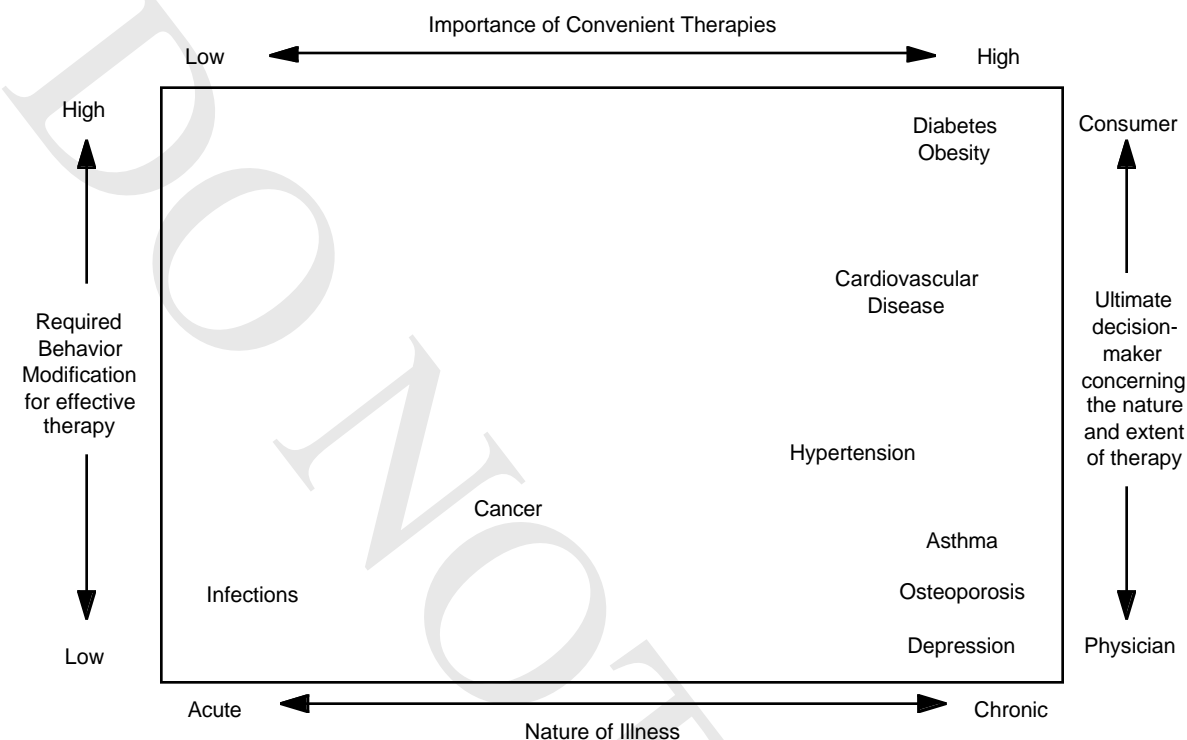
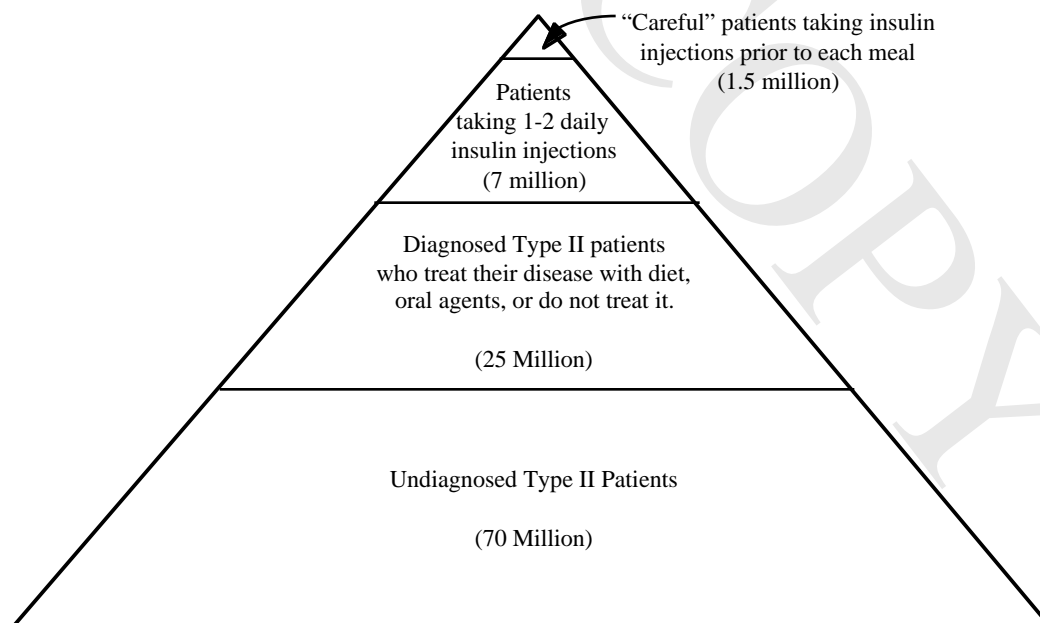
	Europe, Middle East & Africa	North America	Japan	Rest of World	Total World Market
<b>1994 Revenues (US\$ millions)</b>					
Eli Lilly	123	456	50	25	744
Novo-Nordisk	450	132	123	33	741
Hoechst	137	0	0	0	137
Others	0	0	3	6	9
Total Market	710	678	176	64	1628

**Market Shares by Region:**

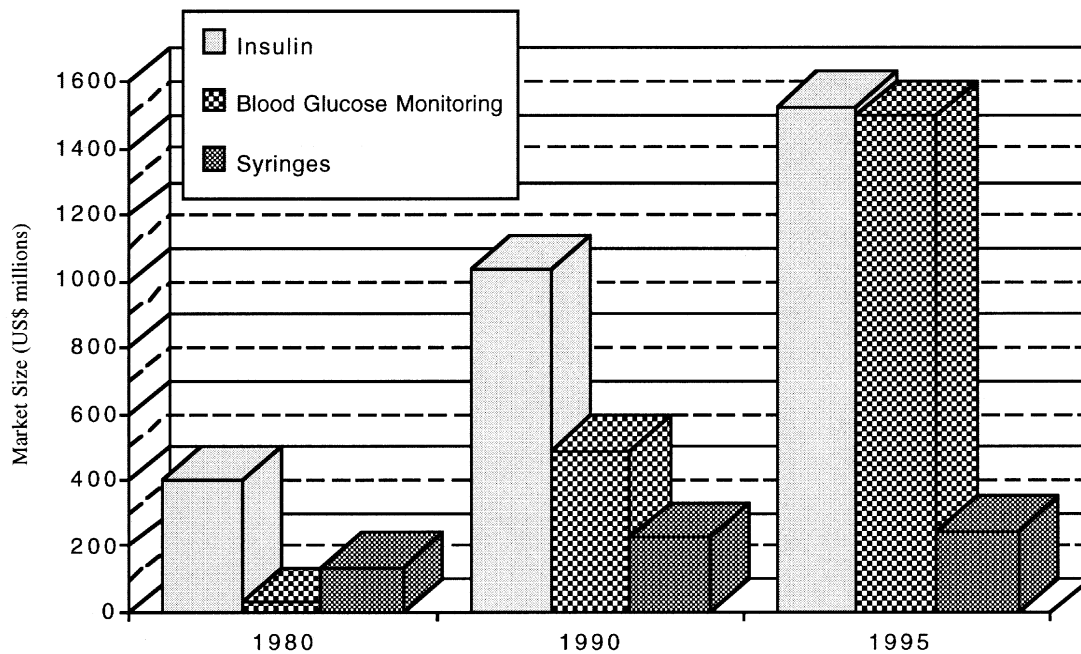
Eli Lilly	17%	80%	28%	38%	46%
Novo Nordisk	64%	20%	72%	52%	45%
Hoechst	19%	0%	0%	0%	8%
Others	0%	0%	0%	10%	1%

Note: Data in this table represent the casewriter's estimates, based on data from several sources.

**Exhibit 5:** Differences in the Rates of Flow of Insulin and Glucose into the Bloodstream

**Exhibit 6:** A Map of Key Characteristics of Prominent Diseases**Exhibit 7:** Percentages of Patients at Each Stage of Therapy



**Exhibit 8:** Growth of the Blood Glucose Monitoring Market, Compared to the Insulin Market

Source: Casewriter's estimates, synthesized from numerous sources

**Exhibit 9:** Changes in Market Shares of Eli Lilly & Co. vs. Novo-Nordisk, 1980-1995

	Europe	North America	Rest of World	Total
Eli Lilly -- 1980	0%	89%	28%	53%
-- 1995	17%	80%	31%	46%
Novo -- 1980	50%	0%	48%	24%
-- 1995	64%	20%	65%	45%

Source: Casewriter's estimates, synthesized from numerous sources