DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 15(10), 1555-1575 (1989)

JAPAN'S GROWING PHARMACEUTICAL INDUSTRY

-- A THREAT TO THE UNITED STATES ?

Suneeta Banakar and Umesh Banakar*

Creighton University
School of Pharmacy & Allied Health Professions
Omaha, NE 68178-0230

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I. INTRODUCTION

One of the few areas where U.S. companies still hold the upper hand over Japan is in pharmaceuticals. U.S. pharmaceutical companies rang up

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*To whom correspondance should be addressed.

a trade surplus with Japan of about $300 million in 1984 (Helm 1985). However, Japan has become a leading force in pharmaceutical innovation and marketing. Western pharmaceutical companies short of new drugs are increasingly turning to Japan for ideas. Ten years ago this would have been impossible : the Japanese drug industry then had no products of its own. Japanese companies were content to rely on the west to discover the drugs, and to grow on the profits generated by manufacturing and distributing them in their home market.

How did the Japanese pharmaceutical industry become a leading force in the world pharmaceutical market? This paper will examine the growth of the pharmaceutical industry in Japan taking into consideration the environment, government regulations, export/import regulations, and other factors affecting the industry. Further, the paper will also discuss the implications of the growing Japanese pharmaceutical industry for the United States.

II. GROWTH OF THE JAPANESE PHARMACEUTICAL INDUSTRY

II. A. Background

There are about 2,000 pharmaceutical companies in Japan with an annual output of approximately 4 trillion yen. Many of these pharmaceutical companies, however, are too small to develop new products or to sell overseas on their own. About 80% of the pharmaceutical firms in Japan have a capital of less than 100 million yen and 90% employ fewer than 300 workers (Onishi 1985). The top ten Japanese pharmaceutical manufacturers and their sales in millions of dollars are shown in Table I.

TABLE I

JAPAN'S TOP TEN PHARMACEUTICAL MANUFACTURERS

(fiscal year ended April 1984)

Company	Dollars (millions) Sales	Net profits
Takeda Chemical Industries	2,135	93
Sankyo	1,038	40
Fujisawa	910	49
Shionogi	792	43
Tanabe Seiyaku	639	20
Eisai	604	27
Yamanouchi Pharmaceutical	480	29
Chugai Pharmaceutical	447	20
Daiichi Seiyaku	364	16
Banyu Pharmaceutical	308	10

Pressure from competitors has forced Japanese companies to look at foreign firms for help. Only a handful of Japanese firms have been able to set up subsidiaries or joint ventures in America and Europe although the trend is rapidly on the increase (The Economist 1983a). The Japanese pharmaceutical market is the second largest in the world after the United States. The Japanese antibiotics market is worth about $4 billion and is very competitive (The Economist 1983b). However, until recently, the market had been a tough one for European and American companies to cultivate.

II. B. Increase in Sales

Until a few years ago, Japanese drug companies depended on drugs originated by foreign companies. They either imported the products, manufactured them under license from U. S. or European makers or imitated them. Then things began to change, and now the Japanese are powerful players in the drug game. The Japanese are now developing 20% of all new drugs versus only 1% ten years ago. In 1982, for the first time, they licensed more products for distribution abroad than they brought in. Morever, they received 38% of the patents granted by the United States to foreign pharmaceutical companies in 1982.

The output of pharmaceutical products after World War II and the rate of increase of production compared to the previous year is shown in Table II. In general the growth rate of the industry has been very high, but there has been a slackening after the explosive expansion immediately after the war. The average growth rate was 18.5% in 1955 - 1964, 15.2% in 1965 - 1974, and 10.0% after 1975 (Nitta 1984).

As in other professional areas, the Japanese government played a crucial role in the development of the Japanese pharmaceutical industry. Its actions have shaped the market including the pace and nature of new drug development and the industry's overall infrastructure. In the 1960s, the government introduced national health insurance, triggering a huge increase in consumer demand for pharmaceutical products. The market grew so rapidly that by 1982 the Japanese per capita bill of $ 95, largely government paid, was the world's largest. Consequently, the Japanese pharmaceutical market reached $12 billion in 1982 - the second largest in the world, after the U.S. with $19 billion annually (Sender 1983).

TABLE II

JAPANESE OUTPUT OF PHARMACEUTICAL PRODUCTS : 1945 - 1983

Year	Production Output (million yen)	Rate of Increase compared with previous year
1945	335	
1946	1,872	
1947	5,176	176.5
1948	17,902	245.9
1949	31,031	73.3
1950	31,916	2.9
1951	42,376	32.8
1952	58,564	38.2
1953	75,647	29.2
1954	78,468	3.7
1955	89,539	14.1
1956	103,767	15.9
1957	125,147	20.6
1958	134,476	7.5
1959	149,258	11.0
1960	176,012	17.9
1961	218,075	23.9
1962	265,596	21.8
1963	341,141	28.4
1964	423,225	24.1
1965	457,639	8.1
1966	507,108	10.8
1967	563,257	11.1
1968	688,953	22.3
1969	842,514	22.3
1970	1,025,319	21.7
1971	1,060,424	3.4
1972	1,091,791	3.0
1973	1,367,138	25.2
1974	1,699,688	24.3
1975	1,792,406	5.5
1976	2,162,436	20.6
1977	2,458,294	13.7
1978	2,793,878	13.7
1979	3,042,302	8.9
1980	3,482,177	14.5
1981	3,679,139	5.7
1982	3,980,232	8.2
1983	4,032,057	1.3

However, the Japanese pharmaceutical industry could not capitalize on the giant market because Japan did not have any meaningful patent laws. Without them, companies were reluctant to spend money on research in the fear that their developed product would be pirated by competitors. In 1976, the government became aware of its growing trade deficit in pharmaceuticals. This proved to be beneficial to the pharmaceutical industry of Japan. To spur local pharmaceutical development and manufacturing (production), the government introduced strong patent protection and altered the pricing system of drugs. Tokyo established higher prices for newly developed products making innovation lucrative.

The results were dramatic. Research and development spending as a percentage of sales soared even as sales rose. Technology started to flow from East to West, and new drugs gave the Japanese the means to establish themselves abroad, particularly in the United States.

In their own efforts to ensure the industry's growth, Japanese pharmaceutical manufacturers are increasing their dependence upon R & D, specifically projects that will develop products with annual sales over $40 million. "We no longer feel that we cannot compete with companies in America or Europe in antibiotics, drugs for the circulatory system, cancer drugs and others," says Yoshibumi Kawamura, president of Sankyo Pharmaceutical (Ushio 1985).

II. C. Innovation and Research and Development

Japanese pharmaceutical companies excel in the development of antibiotics largely attributed to the fact that antibiotics account for 24% of domestic sales (Business Week 1982). Japanese pharmaceutical

firms are among the leaders in perfecting so-called third generation cephalosporins. These are stronger, safer and are effective against a wider range of bacteria than their predecessors.

A major trade deficit with the U.S. is behind the Japanese push into drug development. Japan's trade deficit has grown while domestic sales have nearly tripled in the past ten years. This is illustrated in Figure 1. Almost 80% of the drugs and related products sold in Japan continue to be manufactured overseas or produced locally from technology developed outside Japan. But the Japanese are fast catching up. In 1982, the Japanese pharmaceutical industry devoted $775 million to research and development, a gain of about 10% over 1980.

Japanese pharmaceutical companies are coming up with innovative products. In the past two years, of the 104 new drugs launched on to the world market, 26 originated in Japanese laboratories. Ten years ago none did. The amounts spent on research and development by Japan's top 16 pharmaceutical companies from 1967 to 1980 are depicted in Table III.

The types of drugs being developed are changing as well. Previously, Japanese companies tailored their drugs to Japanese diseases. But with an eye on foreign markets, they have started to look at drugs which treat "western" diseases, like heart attacks. At the same time, the ailments Japanese suffer from have begun to change. For instance Japanese now live longer, therefore ailments like arthritis are more common. Also, the proportion of the population suffering from heart and circulation diseases has doubled to 4% since the early 1970s. Responding to these changes the Japanese companies are increasingly researching the same areas as are the western giants (The Economist 1983b).

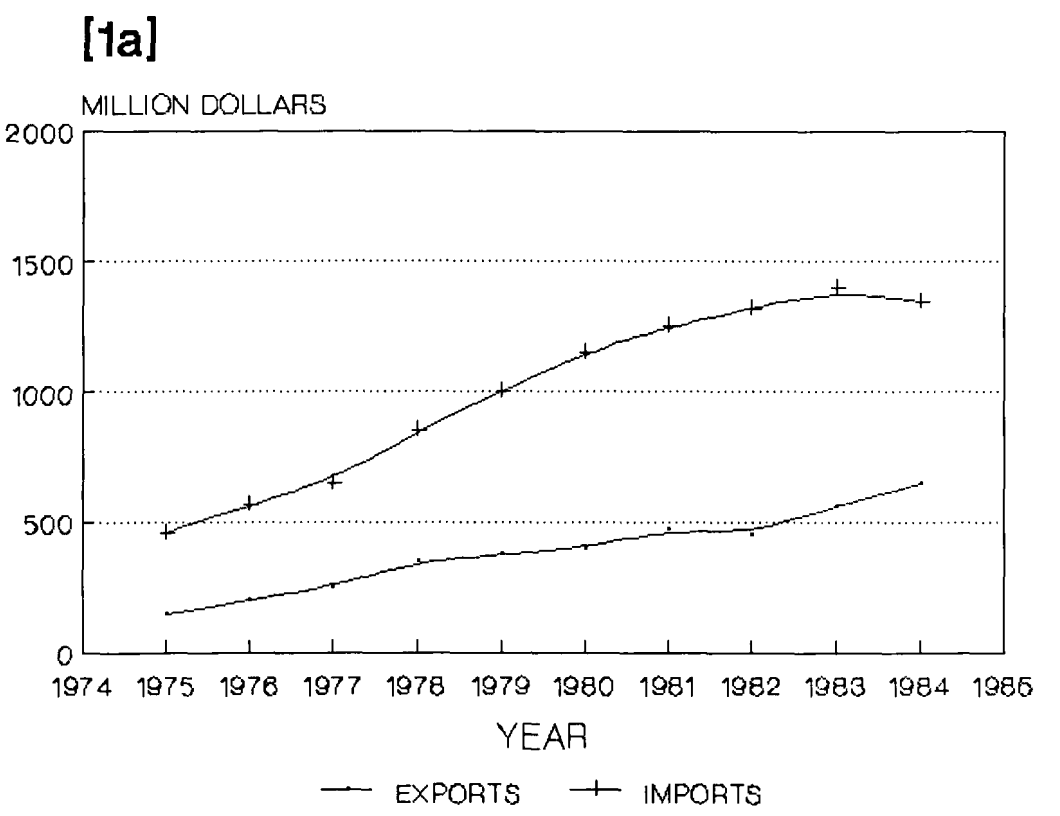

Fig.1. Japan's Pharmaceutical Trade Deficit (1a) for the decade 1975-1985, and the Growth in Domestic Sales (1b) during the same Period [Sources: Japan's Ministry of Finance and Ministry of Health and Welfare].

The thrust of Japanese research is concentrated on three main categories, including antibiotics, anti-cancer drugs and heart disease agents. Some specialty areas are also being pursued, such as artificial blood, etc. But its in the area of biotechnology where Japan, admittedly several years behind the U.S., may achieve significant breakthroughs.

The Japanese are recognized as world leaders in the development of fermentation technology - needed for the mass production of genetically

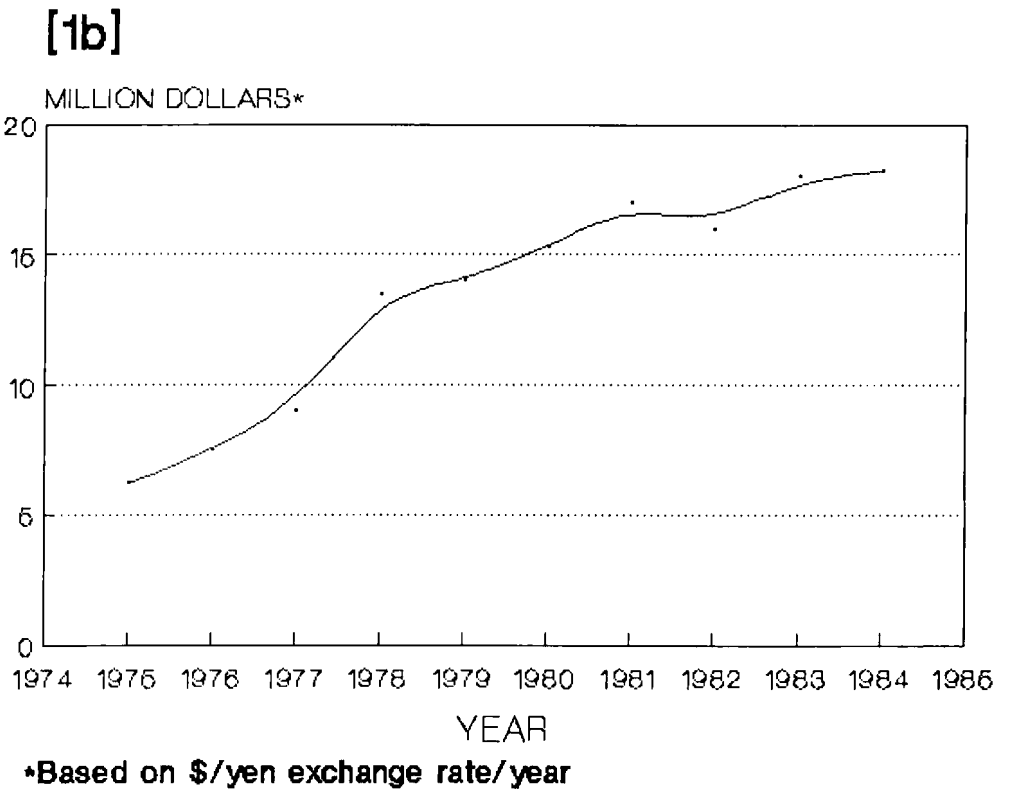

FIGURE 1 CONTINUED

engineered organisms. A number of more aggressive Japanese companies have taken stock ownerships in some U.S. genetic engineering firms and are conducting joint research projects and exchanging technology for mutual benefits (Sharon 1981).

An analyst at Drexel Burnham Lembert, Robert Schmitt, who has been following the Japanese industry for 16 years believes Japan is now preeminent in anti-cancer drugs, certain antibiotics, and artificial blood (Curtis 1981). Says Schmitt, "They are gearing up to become a world leader."

TABLE III

RESEARCH AND DEVELOPMENT BY THE TOP 16 JAPANESE PHARMACEUTICAL COMPANIES : 1967 - 1980

Year	R & D Expenditure in millions of yen	% Change
1967	12,724	
1968	13,924	+ 9.6
1969	16,611	+19.1
1970	20,699	+24.6
1971	26,176	+26.5
1972	30,584	+16.8
1973	35,090	+14.7
1974	42,048	+19.8
1975	51,329	+22.1
1976	57,091	+11.2
1977	65,331	+14.4
1978	72,223	+10.5
1979	83,870	+16.1
1980	98,598	+17.6

However, research and development of pharmaceutical products in Japan still center on improvements of existing products. Introduction of new products based on original research are still to be introduced.

II. D. Government Regulations

Drug regulation in Japan became formalized with the enactment of the Pharmaceutical Affairs Law (PAL) in 1960 (Scrip World Pharmaceutical News 1981). This law established a Ministry of Health and Welfare (MHW)

to oversee pharmaceutical regulatory affairs. The MHW has the power to investigate the safety and effectiveness of drugs based upon an application for an individual manufacturing approval. Within the MHW, supervision of the pharmaceutical industry is the responsibility of the Pharmaceutical Affairs Bureau (Reich 1986).

Perhaps the most powerful body within the drug regulatory system in Japan is the Central Pharmaceutical Affairs Council (CPAC). This group provides counsel to the MHW concerning drug regulatory policies and their implementation as well as exercising final approval over all new drug registrations (Pradhan 1975).

Japan revised the PAL in 1983 in an effort to reduce trade barriers. Under the 1983 revision, foreign based pharmaceutical firms can apply directly to the MHW for a manufacturing approval. Once the approval is acquired, a local Japanese importer can be contacted to file an application for an import license.

The government's policy on pharmaceuticals is a major cause for concern to both foreign and national manufacturers in Japan. The government controls the pricing of prescription products which account for approximately one-third of total medical expenses in Japan. Uncontrolled over-the-counter (OTC) drugs account for only a minor share of total drug sales, and that share has been decreasing steadily for more than a decade.

The government funded health program, to which almost all Japanese belong, pays doctors little for office visits but pays them handsomely for dispensing drugs. The health ministry sets prices for drugs prescribed on the national insurance service. Hospitals and doctors then negotiate aggressively with distributors demanding discounts of 30% or more although the government reimbursement is based on the full price.

The extra cash is pocketed by the hospital or doctors - it is their main source of income.

Doctors typically run their own dispensaries. Say a doctor prescribes antibiotic X. He pays a wholesaler 60 cents a capsule, 50 cents of which the wholesaler passes along to the manufacturer. The government pays the manufacturer $1 a capsule, the official reimbursement price. So the doctor makes 40 cents (Smith 1985).

Due to the inherent nature of the system, the temptation to overprescribe is irresistable. A stock joke in the health industry is that when a patient goes to a doctor and complains of a cough, the doctor automatically orders up an antibiotic. He also prescribes cough medicine, then vitamins because the patient seems a little run down. Finally, the doctor orders something to coat the stomach because the patient has been taking too many drugs.

Such overprescribing has aggravated government deficits. Japan's national expenditure on medical care has increased about 40 times over the 25 years since 1961 when the national health insurance system was introduced (Watanabe 1986). The cost of health care in Japan accounts for 5% of GNP - smaller than the U.S. figure of 11% - but a problem nonetheless.

Starting in 1981 the government began adminstering shock therapy to the drug industry. The health and welfare ministry slashed reimbursable prices by an average of 18.6% and has started reviewing prices annually, instead of every three years. For the most part, drugs that are shown to get people better, safer and faster, and presumably inexpensively in the long run, can still command a high reimbursement price. However, manufacturers of generic drugs and of drugs that are slight variations of other successful products will have to get out of the business or become more inventive (The Economist 1982).

The Japanese government, which usually protects industries too weak to stand up for themselves, has been wary of letting foreign firms into the Japanese pharmaceutical market. The pharmaceutical industry in Japan is fragmented with only one firm, Takeda Chemical Industries, ranking among the world's top 20 producers. Upto the early 1980s, rules on imports protected inefficient firms and high drug prices helped to keep hundreds of small companies in business.

This current state of affairs is changing rapidly. Under pressure from the U.S. and the European Economic Community, most controls on direct foreign investment and some restrictions on imports have been relaxed. Foreign firms patents have been given the same protection enjoyed by Japanese pharmaceutical companies.

III. PROBLEMS FACING THE JAPANESE PHARMACEUTICAL INDUSTRY

III. A. Increased Corruption

Due to the intense competition prevailing in the Japanese pharmaceutical industry, several Japanese pharmaceutical firms have been caught faking their clinical data in order to get new drugs on to the market quickly. With new drugs costing $50 million or more to develop, the pressure on small companies is immense and cutting corners is almost a matter of survival.

Nippon Chemiphar, trumpeted as one of Japan's up-and-coming drug makers, with annual sales topping $100 million was shut down for 80 days following a government inquiry into irregularities in its application for permission to market its Norvedan painkiller and its Toscarna drug for hypertension. Another example is the Osaka based Green Cross Company who had its application for marketing an artificial blood product bounced for similar reasons. In both instances, it was a disgruntled former employee who spilled the beans (The Economist 1982).

Toyama Chemical is another Japanese pharmaceutical company whose members of the senior staff were accused of industrial espionage (The Economist 1983c). In an unusual twist, the Toyama employee was accused of bribing an official of the ministry of health to steal information about an antibiotic being developed by another company.

Japanese pharmaceutical regulators can take administrative steps to stop the most straightforward thefts of commercially sensitive research information. The national health institute employs hundreds of temporary staff - many of whom see such data, but are not bound to keep it confidential. The institute is belatedly considering ways of making such information more secure.

III. B. Environmental Conditions

The environment surrounding the health care industry in Japan is changing rapidly. With the inevitable advent of an aging society in which older people predominate, the need for pharmaceutical products is expected to undergo a fundamental transformation. The transformation is dependant upon changing patterns of diseases with the increase in chronic adult diseases.

The discovery of new effective substances has become ever more difficult in view of the long period and large cost required for research and development of new pharmaceutical products. Therefore, a steadily growing outlay of time and money are needed for studies of the effectiveness and safety of new products about to be released on the market (Nitta 1984).

A period of about ten years and costs of billions of yen are regarded as necessary for the development of a single new pharmaceutical product. This tendency is expected to become even more pronounced in the future. Investments in a development project are getting harder to

recover, for example, in conjunction with the shortening of the patent life.

Stiffer competition from the multinationals is also hurting Japan's pharmaceutical manufacturers, just when they thought they were getting good at innovation. Profits at three of the four large Japanese drug firms fell in 1985. Japanese pharmaceutical firms are reacting to this squeeze by improving their research and development (The Economist 1985).

IV. IMPLICATIONS FOR THE U.S. PHARMACEUTICAL INDUSTRY

IV. A. U.S. Companies In Japan

Until 1975 foreign drug companies were barred from owning manufacturing operations in Japan, and most companies entered the market through licensing agreements or joint ventures (Chemical Week 1982). U.S. pharmaceutical manufacturers believe that the only way to survive and prosper in Japan is to become part of the domestic business climate by establishing their own research production, and marketing bases in Japan (Smith 1985).

Since the relaxation of rules of investment by the Japanese government, more and more companies have been quick to take advantage of this Japanese hospitality. In 1979, accumulated investment by foreign pharmaceutical companies in Japan was about $100 million. By 1982, that had doubled. For example, in 1983, Merck, an American pharmaceutical firm made the largest single foreign investment in the Japanese drug industry by paying $350 million for a controlling interest in Banyu Pharmaceuticals (Business Week 1983). This gave Merck 4 - 5% of Japanese drug sales. In 1985, Dow Chemical Co. subsidiary bought a 17% stake in Funai Pharmaceuticals Ltd., a small Japanese company. Upjohn Co. has

invested more than $50 million in a research and manufacturing facility north of Tokyo. Searle and Co. will also begin manufacturing in Japan soon (Helm 1985).

In March 1985, U.S. trade officials specified three issues they considered damaging to pharmaceutical trade with Japan :

(i) Japan's unwillingness to accept foreign clinical test data for pharmaceuticals to be made or sold in Japan;

(ii) lack of "transparency" in the process by which drugs are approved in Japan; and

(iii) unwillingness of the Japanese government to permit transfer of licenses from U.S.-Japanese joint ventures to wholly U.S. owned manufacturing ventures for the production of an identical product. A result of such a policy is that the U.S. company must reapply for a license and may encounter a delay of two or more years (Ushio 1985).

The Pharmaceutical Manufacturers Association (PMA) has been working with the Japanese government and its pharmaceutical industry on the trade issues since 1979, but without much success until 1985 when negotiations between the two governments were initiated. The head of the U.S. delegation, David Mulford says Japan agreed to :

(i) accept the results of non-Japanese clinical data in approving pharmaceuticals except when there may be differences between how Japanese and foreigners react to a drug, or where an entirely new substance is used as a diagnostic indicator;

(ii) allow transfers of licensing approvals for products or manufacturing units from one business to another;

(iii) adopt and publish standard processing periods for any applications submitted on pharmaceuticals;

(iv) list prices quarterly for all new drugs and make public the formulae used for calculating the prices;

(v) cut the period for examining new drug applications from 30 to 18 months;

(vi) allow direct communication between pharmaceutical firms and regulatory authorities on technical matters.

Both foreign and Japanese producers will be helped by the agreement, especially the provision that allows consultation with the government. Previously companies were not even allowed to ask the Central Pharmaceutical Affairs Council why an application was rejected (Rhein 1986).

IV. B. Japanese Products In The U.S.

Green Cross, a middle sized Japanese company started selling artificial blood in the U.S. market - a major pharmaceutical breakthrough in 1981. Sankyo, based in Japan, is already a leader in anti-cancer drugs. Two of the best new antibiotics to come on the U.S. market were developed by Shionogi and Fujisawa (Curtis 1981).

Increased research and development gave the Japanese the means to establish themselves abroad, particularly in the United States. American pharmaceutical manufacturers, eager for new products to sell at home, became willing salesmen for the Japanese. By 1983, virtually all the major companies had arrangements to market Japanese drugs in the United States. Abbott Laboratories signed up to market products for Takeda Chemical; Eli Lilly & Co. is marketing antibiotics for Shionogi; and SmithKline Beckman gave Japanese marketing rights for Tagamet, the world's largest selling drug, to Fujisawa in exchange for three new antibiotics (Sender 1983).

Indeed, U.S. companies have actively pursued licensing agreements with the Japanese pharmaceutical manufacturers, motivated by their unceasing appetite for new products and the uncertainties of success in their own research efforts. "Because there is never a guarantee that a drug under development will prove both safe and successful," explains Executive Vice President, Edward Roberts of Eli Lilly & Co., "licensing is an insurance policy."

The competition among American firms to form relationships with Japanese pharmaceutical manufacturers is intense. American companies have been scouring Japan to find out what the local companies are up to and how productive their research efforts may be. Thus, both Japanese and American companies are advancing the introduction of Japanese drugs in the U.S. market.

Japanese companies are also moving to establish footholds in foreign countries, especially the United States. Fujisawa Pharmaceutical established a joint venture with Smithkline Beckman in 1981. Takeda Chemical Industries is another leader in overseas investment. The company recently upgraded the drug development partnership that it established with Abbott Laboratories in 1977 to a $12 million joint venture (Ushio 1985).

V. CONCLUSIONS

Despite the increased research and development and innovations, Japanese pharmaceutical firms do not yet seem ready to set up shop abroad. Unlike the situation with cars, drug production costs, particularly for labor, are far less critical, so the Japanese gain no special advantage as exporters. Secondly, marketing of pharmaceuticals in the U.S. requires a super-sophisticated sales force. Finally,

government regulations, particularly the lengthy process involved in getting the Food and Drug Administration's approval, makes competing in pharmaceuticals very different from other industries.

So far the Japanese have been well served by licensing agreements. Chugai Pharmaceuticals, for example, is one of the most promising and says it prefers to rely on income from licensing while it learns the tricks of the trade in the west (The Economist 1983b). The Japanese recognize that they lack managerial and marketing ability to exploit the U.S. market. However, collaborations have enabled them to use local management and have served as excellent training grounds to acquire the skills needed for expansion in the U.S.

Thus, the Japanese challenge in pharmaceuticals has begun. If the present trend continues, Japanese products in the next few years will gain an increasingly significant foothold in the American market.

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