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The purpose of this study is to delineate the chief factors in the foundation of a modern Japanese pharmaceutical manufacturing industry by tracing its gradual shift from the production and marketing of existing medicines to the research and development of innovative drugs. The factors which led to this transition are: (i) health care policies and regulations, (ii) technological innovations, including both novel manufacturing and medicinal technologies and (iii) entrepreneurial initiative. To elucidate the transition process, the writer will examine the historical development of Yamanouchi Pharmaceutical Company (abbreviated below as Yamanouchi). The scope of the study is from 1923, the year of the company’s founding, to the 1976 patent reform, which recognized product patents. Although there are many other policies to consider, this piece of legislation provided the most important catalyst for the birth of innovation in the Japanese pharmaceutical industry as it necessitated a fundamental change in the approach to product development.

With regard to literature on the development of the Japanese pharmaceutical industry, this sector has not enjoyed the popularity
among business historians as some others. In Japanese, one can find analyses that explore the industrial development process as well as related historical background and societal issues. Corporate histories, some covering a century or more of operations (Tanabe, Takeda, Sankyo, Shionogi, etc.) provide another point of reference, though most, but not all, offer little in terms of analysis. Although not academic works, there are accounts written by or about the contributions of entrepreneurs/scientists that provide the business historian with another perspective.

In studies on the development of the pharmaceutical industry as a whole, western scholars, including some business historians, have mentioned prominent Japanese scientists such as Jōkichi Takamine. However, they have placed greater emphasis on Japanese contributions to the history of medicine than to the pharmaceutical business. Perhaps


3. Too numerous to enumerate, corporate histories are published by most major Japanese pharmaceutical manufacturers and some foreign affiliates. The following is one of the few that does offer an analysis. Nihon Rekishi Kenkyū-sho, eds. *Ban’yū Seiyaku 80 Nenshi* [An Eighty-Year History of Ban’yū], (Tokyo: Ban’yū, 2002).


one reason for the dearth of historical research in English language is that Japanese pharmaceutical manufacturers have remained small in scale and less globally-present than either their European or American counterparts. It is hoped that this study will provide new insight into the development of this industry, especially for those to which works in the Japanese language are inaccessible.

Background

One of the distinctive features of Japan's case is its history of embracing two fundamentally different traditions of medicinal science and technology, the first one originating in China and the second, in Western Europe. While trade in traditional remedies flourished over centuries, the initial attempts to manufacture western pharmaceuticals did not get underway until the late-1800s. The firms comprising the Japanese industry in the early days came from a diverse variety of backgrounds. Among the first to enter the industry, what might be considered the first movers, were not originally producers of western medicines but medicinal wholesaler-merchants (yakushu ton’ya) whose imported medicinal herbs were transported and sold through complex sales networks extending across a relatively limited geographic region. The most considerable cluster of wholesaler-merchants could be found in Doshōmachi in central Osaka, although there were other areas of the country with a strong reputation in the medicinal trade. Because these

Though only his scientific contributions are cited, Takamine was also an adept entrepreneur.

6. According to the following, Japan was a latecomer due to the long period of isolation (sakoku). Masaru Wada, *Iyakuhin Sangyōron* [The Pharmaceutical Industry], 22. Even today, the largest Japanese manufacturer, Takeda, ranks 14th worldwide in terms of sales. *Yakuji Handobukku* [Pharmaceutical Affairs Handbook] (Tokyo: Johō, 2004), 181.

7. The Japanese pharmaceutical industry is comprised of firms from a wide variety of backgrounds, including sectors completely unrelated to the production of medicine. The following provides an analysis of the formation of a Japanese pharmaceutical industry. Yongue, 5-70.


9. Even before the start of the Meiji period, Osaka was Japan’s foremost center for all
origins, their primary comparative advantages were their well-established networks of small affiliated enterprises, extensive capital assets and consumer trust built over many years of operations, not their novel medicinal or production technologies or economies of scale.10

The introduction of western medicine and the efforts to foster a viable industry came about as part of a wider government initiative to modernize the nation according to a western model. In this process, policy was of defining importance. Among the measures put in place, a Japanese translation of the pharmacopoeia (the first in Asia) in 1886, direct subsidies to industry through the implementation of the 1885 Industrial Fostering and Encouragement Policy (Shokusan Kangyō Seisaku) and the creation of state-funded pharmaceutical enterprises had the greatest direct impact on this nascent industry.11

These government policy initiatives were significant first steps in the building of a viable industry; however, they in themselves were insufficient. In the early years, public enterprises failed, while relatively few private firms joined.12 Japan’s reliance on imports persisted since medicinal products of mainly German origin were not only lower in price, but also of superior quality to those produced domestically.

The interruption of imports from Europe at the initial outbreak of World War I followed by grave shortages of pharmaceutical products

10. The reader may compare the first mover advantages of the Japanese pharmaceutical with those in the following. Alfred D. Chandler, Scale and Scope, The Dynamics of Industrial Capitalism. (Cambridge: Harvard University Press, 1990), 34-36.


12. The following chart illustrates this point. Takeda and Fujisawa, two of the industry’s first movers, actually entered the industry at a later date than some other well-established firms including Tanabe, Ono and Shionogi
due to its protraction made the establishment of a viable industry a political imperative. As in the late-1880s, the government again intervened by implementing the 1915 Dyes and Pharmaceuticals Production Promotion Law (Senryō Iyakuhin Seizōshōreiho), which provided financial incentives to large-scale entrants. This measure coupled with the dire shortage of medicinal products gave birth to an enduring Japanese pharmaceutical manufacturing industry. Yet, it was not until the introduction of novel mass production technologies in the early postwar period that it could be considered a truly modern manufacturing industry.

Characteristics of Yamanouchi Pharmaceutical Company

Kenji Yamanouchi founded Yamanouchi Seiyaku Shōkai as a manufacturer of "new" (western) medicines (shin'yaku) on 23 April 1923 in Osaka. Though located in close proximity to Doshōmachi, then still the largest center of the pharmaceutical trade in Japan, Yamanouchi never functioned as a wholesaler or importer, nor is it generally classified as a Kansai- or Osaka-based enterprise. Kenji Yamanouchi

<table>
<thead>
<tr>
<th>Company Name</th>
<th>Founded</th>
<th>Began Production</th>
</tr>
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<tbody>
<tr>
<td>Tanabe</td>
<td>1678</td>
<td>1877</td>
</tr>
<tr>
<td>Ono</td>
<td>1717</td>
<td>1889</td>
</tr>
<tr>
<td>Shionogi</td>
<td>1878</td>
<td>1892</td>
</tr>
<tr>
<td>*Ban'yū</td>
<td>1915</td>
<td>1915</td>
</tr>
<tr>
<td>Takeda</td>
<td>1781</td>
<td>1915</td>
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<tr>
<td>*Daiichi</td>
<td>1915</td>
<td>1918</td>
</tr>
<tr>
<td>Fujisawa</td>
<td>1894</td>
<td>1918</td>
</tr>
<tr>
<td>Nippon Shin'yaku</td>
<td>1911</td>
<td>1919</td>
</tr>
</tbody>
</table>

*New medicines manufacturer.

13. According to this law, companies capitalized at at least ¥500,000 were eligible to receive subsidies for a period of 10 years. This legislation was highly advantageous to larger enterprises as opposed to those that were just beginning to engage in pharmaceutical production activities. Nihon Yakushi Gakkai [Japanese Society for the History of Pharmacy], eds., 57.

14. One can find numerous examples of studies that classify pharmaceutical manufacturers by place of origin (Kansai, Tokyo), type of product (shinyaku, pharmacopoeia listed, etc.) or by original function of operations (wholesaler, importer, entrant from another industry, etc.). Typologies can be found in the following. Takenori
did not choose to enter the market at a particularly propitious time. Domestic demand for pharmaceutical products sparked by the First World War had waned; moreover, there were no favorable government policy incentives, nor any possibilities of exploiting a novel technology. Kenji Yamanouchi had acquired some knowledge of the medicinal business as he had worked in the pharmacy of a store (Takaki Shōten Yakuhinbu) after graduating from a school specializing in trade and language (Ōsaka Bōeki Gakkō). However, he was first and foremost an entrepreneur—not a scientist—whose sole advantage at that point in time was his strong drive and determination.

There are three reasons for the choice of Yamanouchi in this study. First, for the purposes of this study, which traces the origins of innovation in the Japanese pharmaceutical industry, Yamanouchi provides a representative example. This is not to say that its strategies were identical to those of other enterprises, as they were devised to fit its own specific circumstances. Yet, because Yamanouchi shared the same historical and regulatory environment, it demonstrates many of the same general tendencies of the industry as a whole.

Second, unlike the first movers to the industry, Yamanouchi was not endowed with any outstanding competitive advantages including extensive sales networks or capital assets nor was it particularly innovative at the time of entry. Indeed it is Yamanouchi's comparative disadvantages and its initial lack of novelty that make it the most interesting choice of a study on the origins of innovation. Yamanouchi, the first Japanese enterprise to succeed in producing sulfonamide domestically, provides a clear example of the transition that was beginning to occur in the pharmaceutical manufacturing sector as a whole. The comparative advantages that Yamanouchi did later achieve were derived from two of the factors mentioned in the introduction, technological innovations, procured at first from overseas and developed in-house, and entrepreneurial initiative.

Third, Yamanouchi's case clearly illustrates the importance of entrepreneurial initiative. Kenji Yamanouchi’s style of management was

key to the company’s transition from manufacturer/marketer to innovator. According to corporate documents and numerous interviews with employees, there were three distinguishing characteristics in his approach. First, in an industry dominated by family-owned and managed enterprises, Kenji Yamanouchi’s management philosophy was clearly egalitarian as it incorporated promotion based on ability rather than family or academic background. Second, he placed particular emphasis on strengthening two business areas, marketing, which included the establishment of strong distribution channels, and quality control. Third, he continually strove to enhance the quality of his organization by remaining keenly attuned to outside developments. This can be illustrated by his interest in collecting scientific data throughout Japan as well as from overseas, recruiting a prominent specialist from the outside, and from the start of operations, seeking ways to internationalize.

Egalitarian Management Style

From the time of the company’s founding, the corporate culture at Yamanouchi was different from many other Japanese pharmaceutical manufacturers, where descendants of the original founders held or still hold important administrative positions. Although Kenji Yamanouchi continued to retain a high post during his lifetime, he preferred, whenever possible, to place his most competent staff in charge of the actual management of the company. Because of his stance, it can be said that he provided a new style of leadership, which embraced a more egalitarian philosophy; one that is clearly expressed a speech to new employees. “This company has absolutely no cliques based on high birth or family or university connections; it possesses no factions nor any other select groups...this company belongs to each and every one of you, and its future is entirely in your hands.”

15. There are many large Japanese pharmaceutical manufacturers whose descendants still hold key positions (Takeda, Eisai). The same is also true of some pharmaceutical-related businesses including pharmaceutical wholesalers (Nakakita) and generic drug manufacturers (Tōwa).

Kenji Yamanouchi’s egalitarian management style was also reflected in his rewarding of employees whose endeavors had in some way contributed to the establishment and growth of the company. One such example is that of Takeo Matsushima, whose contact with the company began shortly after it was founded. While still a student, Matsushima worked with Kenji Yamanouchi to promote the company’s first major launch, Camporisin. Upon graduation, he joined the company full-time and was later appointed as Yamanouchi’s first postwar president.

An Emphasis on Marketing

Today, because of the sizeable corporate investment made in the marketing of pharmaceutical products, a medication’s brand name is often synonymous with that of its manufacturer. However, before the start of pharmaceutical marketing in Japan in the 1950s, medicines were considered to be mere chemical substances, which meant that in most cases, consumers made little, if any, association between a drug’s brand name and its manufacturer. Given this situation, it is significant that Kenji Yamanouchi took such a keen interest in marketing, even in the earliest days of operations. Yamanouchi’s first launch was a cold remedy, which was followed in 1924 by Camporisin, a treatment for neuralgia (shinkeitsū) produced from camphor. This product became the company’s first commercial success, thanks to an extensive marketing campaign led by the founder and a few of his employees.

Kenji Yamanouchi’s marketing strategies were highly personalized. First, he sent samples of the product along with handwritten explanations directly to medical institutions all over the country. After the samples had arrived, he had his employees accompany representatives of the wholesaler during their visits to medical institutions. In this way, they were often able to persuade physicians,
who had initially shown limited interest in the product, to make purchases. In some cases, the founder made visits to the institutions himself and even helped to create advertisements, including the layout and wording.

In 1925, Kenji Yamanouchi succeeded in establishing an agreement with two of the country’s largest wholesalers, Tanabe Gohei Shōten (Kansai) and Nakamura Taki Shōten (Kantō). Wholesalers generally possessed a strong sales network in large cities and their environs, where transportation routes were relatively well developed. However, this was not the case in rural parts of the country, where roads were often extremely poor. To increase sales, Yamanouchi’s employees also visited physicians in rural districts located outside the wholesalers’ networks. In this way, they were able to expand sales without competing with their wholesalers. This strategy of aggressively marketing to physicians across the nation, even in local areas, made it possible for Yamanouchi to promote sales of Camporisin beyond all original expectations.

An Outward-Looking Corporate Strategy

According to Arakawa, information concerning Camporisin was even sent to a number of physicians in the United States, where there was reportedly some interest in the product. Moreover, domestic demand for Camporisin further increased once mention of the interest in the United States was included in the handwritten explanations. Takeo Matsushima, mentioned above, was even sent to the United States in hopes of marketing Camporisin there. He arrived in New York City and enrolled as an auditor at Columbia University in order to collect information as well as seek a means of selling the product in the American market. According to an interview with Yōshi Kobayashi, Kenji Yamanouchi had a close acquaintance in the United States, which may have contributed to his desire to expand his operations abroad, even from an early date. The strong emphasis on marketing and

19. Arakawa, 30.
20. Yōshi Kobayashi, special adviser (tokubetsu komon) at the time, worked closely
internationalization, in particular, has remained a characteristic of Yamanouchi even to the present.\textsuperscript{21}

THE EMERGENCE OF YAMANOUCHI AS A MODERN PHARMACEUTICAL MANUFACTURER

The technologies necessary to manufacture three major medical breakthroughs, sulfonamide, hormone drugs and vitamins, were introduced from abroad in the 1930s. These drugs contributed not only to the progress of medical science, but also to the economic development of a viable Japanese pharmaceutical industry. Demand for domestically manufactured pharmaceutical products sparked what has been called the "new medicines boom."\textsuperscript{22}

Why did Yamanouchi choose to develop sulfonamide? The answer is due both to chance and entrepreneurial initiative. According to the \textit{Fifty-Year History of Yamanouchi Pharmaceutical Company}, one of the employees at its Osaka headquarters, Harutoyo Naitō, had learned of the discoveries made by the German scientist, Gerhard Domagk, and research being conducted on sulfa drug development in France. Naitō was able to obtain additional information by making inquiries at Nagoya University as well as at a number of medical institutions. Using the findings, staff at the Tokyo office including Junpei Watanabe (later a president of Yamanouchi) and Yasushi Terai succeeded in producing the same substance in-house in only one month’s time.\textsuperscript{23}

Thanks to the efforts and speed of Watanabe and his staff, Yamanouchi became Japan’s first producer of sulfonamide, which many industry observers considered quite a feat. Though not supported by any statistical data, the following statement serves as a clear indication of Yamanouchi’s perceived level of inventiveness prior to the launch of sulfonamide. In the journal, \textit{Kagaku Chishiki} (Scientific Knowledge), Tokutarō Yasuda, a physician, wrote: “the first firm to succeed in manufacturing sulfonamide in Japan was a second-rate pharmaceutical

\textsuperscript{with President Shigeo Morioka for many years, correspondence, 7 April 2005.}
\textsuperscript{21. Yongue, 148-150.}
\textsuperscript{22. Hasegawa, 57.}
company (seiyaku gyōkai de niryū) by the name of Yamanouchi. What is more surprising is that this was achieved by a team of young, 30-year-old pharmacologists."24

Thus, in 1937, sulfonamide based on the French discovery was called Gerison, while Albasil, based on the German one, was marketed the following year. In those days, because product patents were not yet recognized in Japan, it was relatively easy to launch copies of an original simply by modifying the development process. Following the launch, Junpei Watanabe continued to play a key role in the early growth of the company in a similar way to Kenji Yamanouchi. According to a 7 December 2000 interview with Yōshi Kobayashi, Junpei Watanabe’s entrepreneurial acumen lay in his knowledge of gathering and deciphering data on recent scientific breakthroughs, while Kenji Yamanouchi’s was in developing strategies to strengthen the company’s sales and marketing operations. The complementary talents of these two men were of vital importance to the establishment of operations in the early years.25 Like Kenji Yamanouchi, Watanabe was also highly respected for his fair treatment of employees.26

Yamanouchi contributed to Japan’s achievement of self-sufficiency in sulfonamide, while high sales of the product aided in the stable growth of the company through to the early postwar period when more effective antibiotics began to enter the market. During the War, military demand for all types of pharmaceutical products, particularly sulfonamide, was so high that it was impossible for Yamanouchi to fill all of its orders. A total of 12 new factories were constructed, and by the end of the conflict, it was producing over 30 percent of the country’s sulfonamide.27 Although the company was relatively unknown a decade prior to its launch, Yamanouchi had managed to achieve a favorable reputation as an innovative ‘new medicines’ manufacturer. According to a 6 April 2001 interview with a senior director, Kunio Watanabe, the

26. This is evident from anecdotes recounted in an interview with Yōshi Kobayashi, 17 April 2005.
27. Arakawa, 42
company came to be known to those in the industry as *sulfa no Yamanouchi*, or Yamanouchi, the sulfa manufacturer.  

**Yamanouchi's First Crisis**

Postwar recovery was not a smooth progression for Yamanouchi due to a number of obstacles. First, because of its direct involvement in the war as one of the nation’s largest suppliers of sulfonamide, Yamanouchi was designated as a special accounting company. Consequently, the Occupation Government barred it from operations until November 1948, when it was granted permission to resume production.

Second, just as many other enterprises, Yamanouchi had suffered numerous wartime losses. Yamanouchi had acquired a relatively large overseas network during the war but was forced to relinquish all of its possessions, including its operations in Manchuria and its offices in China, Taiwan, Hong Kong, the Philippines and Singapore. With regard to domestic losses, aerial attacks in the final phases of the War had brought extensive damage to, or in some cases, completely destroyed the production infrastructure. Four of its factories in Tokyo, one in each Osaka and Kobe were completely razed by aerial attacks; however, these were not the most significant losses. Some personnel who had been instrumental in the establishment of the company in the early days had perished during the War, including Naitô, who had aided the company in the decision to undertake the production of sulphonamide.

The immediate aftermath of the War was unmistakably the darkest period in the history of Yamanouchi. Indeed, at one point it seemed that the company might even be forced to abandon its operations. The cause of the crisis was a new version of its original sulfonamide, Neo-Abasil, which was launched in 1947. Administering this product had resulted in a number of deaths. Determining the true medical cause of the deaths is problematic at this point in time as there is no data available other than the testimonies of employees with firsthand knowledge of the situation. In a 7 December 2000 interview with Yōshi Kobayashi, who interviewed a former president of Yamanouchi, Shigeo Morioka, on the writer’s behalf, the type of injections and the medical practices in use at

28. Kunio Watanabe was also a member of the editing committee for the compilation and writing of *The Fifty-Year History of Yamanouchi Pharmaceutical Company*, interview, 6 April 2001.
that time probably played a role in aggravating the side effects of the medication.29

As a result of the incidents, Yamanouchi was caught in a vicious circle: it was facing legal allegations from victims’ families. However, because Neo-Abasil had been its mainstay, there were few alternative products to generate new revenues as a means of providing financial compensation. With the sudden decrease in available funds, the company could not remunerate its factory employees for their labor, which in turn led to a sharp decline in output. Moreover, a lack of funds also meant that the company would be unable to develop any new products.30 Yamanouchi’s designation as a special accounting company coupled with Japan’s desperate early-postwar economic situation only added to the gravity of the crisis.

According to Kobayashi, the company was on the verge of bankruptcy and without Kenji Yamanouchi’s contacts at Sumitomo Bank, who agreed to a loan without collateral, the company would have undoubtedly been forced to cease its operations indefinitely. He added that had Kenji Yamanouchi not possessed the exceptional personal qualities that he did—particularly his trustworthiness and deep sense of responsibility—the bank would have never agreed to his request and Yamanouchi Pharmaceutical Company would surely not exist today. Since that time, until Morioka’s term as president, the indebtedness toward Sumitomo Bank was repaid by fostering close ties through the appointment of former high-ranking bank employees to advisory posts.31

Yamanouchi’s Postwar Recovery

Domestic production of penicillin was an important catalyst in the growth of the Japanese pharmaceutical industry. According to

30. Ibid.
31. Ibid. It is interesting to note the existence of Banshō Kaishi—Sōgyōsha Yamanouchi Kenji Genkōroku [A Tribute to the Founder], Third Edition, (Tokyo: Dainippon, 1993). This 368-page book contains anecdotes written by some employees of Yamanouchi in tribute to the founder, Kenji Yamanouchi. Essay titles such as “A Man of Conviction”, “Great leader” and “Warm heart” give the reader a sense of the founder’s personality as well as the deep devotion of his employees.
Kobayashi, the facilities at the Azusawa factory, where Morioka was working as a director, could have easily been used as a penicillin production facility. All that the company needed to do was simply to make the necessary manufacturing equipment purchases, notably the procurement of expensive tanks. Morioka had, along with researchers from other companies, personally received training from T.W. Foster, who had been sent to Japan during the Occupation expressly to supervise and promote the domestic production of penicillin. Nonetheless, he opposed the company’s entry into the penicillin market, and Yamanouchi never undertook in-house production.32

The reason why Yamanouchi never opted to take advantage of the strong postwar demand for penicillin lay in the desperate shortage of investment funds. The obvious reason was the Neo-Abasil incident, which drained the company coffers and prevented its management from contemplating any major investments in expensive equipment or facilities. This, however, was a blessing in disguise as the fruits of penicillin production were for most firms short-lived. During the so-called penicillin boom, a flood of entrants—some from industrial sectors completely unrelated to pharmaceuticals—were able to prosper for a time from the sudden surge in demand for penicillin.33 However, many were soon forced out of the market due to the effects of excessive competition and technological innovations, specifically the discovery of more effective antibiotics.

Managers at Yamanouchi instead concentrated their limited resources on the development of a less costly, low-risk niche drug category, contraceptives, one of which could be procured from an outside source. Yamanouchi’s niche market strategy coincided with the objectives of the Eugenic Protection Law (Yūsei Hogohō) of 13 July 1948, implemented to promote the use of contraception and control population growth. The government had initially authorized only seven companies to sell contraceptive products, one being Yamanouchi, which launched a gel called San-C (with C.C.C. as the logo) in 1949. However, by the time that managers at Yamanouchi were able to mobilize their resources so as

32. Yōshi Kobayashi, senior director, interview with Shigeo Morioka on writer’s behalf, 7 December 2000.

33. Entrants included manufacturers of beer, foods, petroleum, textiles, dairy products, electricity, chemicals, etc.
especially basic. Leading Japanese pharmaceutical manufacturers procured innovative western technologies by establishing licensing agreements with foreign firms, while smaller firms probed for alternative methods of producing the same or similar substances using modified or abbreviated processes.

On the other hand, modernizing manufacturing capabilities by means of introducing the latest mass-production technologies was in those days an equally, if not a more pressing need. The gradual improvement of manufacturing methods and equipment made it possible for firms to increase the volume of output, and in later years, to enhance the levels of both quality and safety in their factories. Improvements in manufacturing technologies coupled with the implementation of National Health Insurance (NHI) in 1961 contributed to the sustained growth of the industry as a whole. NHI, in particular, gave a boost to industrial expansion as it guaranteed the provision of healthcare to all Japanese citizens, including medications.37

The Introduction of Foreign Technologies

The first opportunity to launch a new mainstay product came to Yamanouchi somewhat by chance. A manager happened to notice the mention of Sulfisokisasol in a newspaper and was given permission to investigate it.38 Then in a relatively short time, Yamanouchi's scientists succeeded in producing the drug at the Hasune Factory. However, because Hoffman La Roche (abbreviated below as Roche) already possessed the international patent rights for the product, managers from Yamanouchi needed to negotiate with local representatives to establish an agreement to manufacture and market it in Japan. In 1951, the management at Roche, whose policy it was to award patent rights to two Japanese companies, agreed to grant Yamanouchi and Shionogi the exclusivity to manufacture their drug, Saiasin.

Saiasin was an innovative sulfa drug, which it was later discovered, was also effective in the treatment of tuberculosis, a relatively common

37. Following the implementation of NHI, the ratio of expenditures for medications as a ratio of total costs continued to rise in Japan to levels higher than in other developed nations. Some reasons were systemic such as the drug pricing system, special provisions for the elderly and the financial incentive for physicians to prescribe, etc.
38. Arakawa, 59.
disease in Japan at that time. This timely discovery helped to promote the steady growth of Yamanouchi during the 1950s, which was followed by a surge in revenues after 1965 when the government approved the drug for NHI reimbursement. In this way, Saiasin, launched in 1951, became Yamanouchi’s first postwar mainstay product.

Shortly after an agreement had been negotiated with Roche, one of Yamanouchi’s employees, Ryōtarō Okuda, was sent to Germany with the objective of obtaining an agreement with a leading pharmaceutical manufacturer, Boehringer. According to Arakawa’s account, the owner, C.F. Boehringer, had reservations about entrusting the sales of his antibiotic, Paraxin, to such a small firm, and after lengthy discussions, their negotiations reached a deadlock. Just before his departure for Japan, Okuda made a final attempt by mentioning the successful arrangement with Roche in hopes that Boehringer would reconsider his decision. C.F. Boehringer verified the existence of the arrangement with the managers at Roche, who attested to Yamanouchi’s reliability as a licensee. Having thus won Boehringer’s trust, Yamanouchi was awarded the rights to market Paraxin in Japan.39 At approximately the same time, Fujisawa signed a similar agreement with an Italian firm that had conducted joint research on the drug in question with Boehringer. Because Yamanouchi and Fujisawa had both obtained the licensing rights for the same product, they formed a production association (seisankumiai) to oversee the manufacturing of this drug for the Japanese market.

Licensing Conflicts

According to a 7 December 2000 interview with Yōshi Kobayashi, prior to the patent legislation reform of 1976, lawsuits between pharmaceutical manufacturers were not uncommon.40 Shortly after the conclusion of the licensing agreement, Sankyo, then a considerably larger firm, sued Yamanouchi over its launch of Paraxin. Kobayashi stated that the conflict between Sankyō and Yamanouchi did not actually originate in Japan and could be traced to the one between Boehringer and Parke Davis, which had launched the same product.41

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40. Yōshi Kobayashi, interview, 7 December 2000
41. Ibid.
Davis’s licensee, Sankyo, brought its case against Yamanouchi to court, which was followed by five years of proceedings and an amicable settlement.

Despite the protracted legal proceedings resulting from the agreement to market Paraxin, the launch of new products of foreign origin clearly contributed to Yamanouchi’s postwar growth. Moreover, the early trust that was established with foreign licensees through the two agreements helped to foster others. Tranquilizers and sedatives were two of the most important medical breakthroughs of the 1950s and 1960s. Thanks to the fruitful relationship with Roche, new agreements were signed for two tranquilizers, Horizon (Librium) and Balance (Valium).\footnote{Arakawa, 69.} In addition to licensing, research alliances and joint ventures with foreign companies were two other means for Japanese pharmaceutical manufacturers to compensate for the lack of financial and scientific resources. Moreover, they proved to be opportunities for improving innovative capabilities.

The implementation of these strategies and the burgeoning demand for medicines sparked an increase in Yamanouchi’s profits in the early-1950s, followed by only brief periods of deceleration. According to the \textit{Fifty-Year History of Yamanouchi Pharmaceutical Company}, in 1949 capital assets amounted to a mere ¥100 million. However by 1955, sales were close to ¥17 billion and in 1965, exceeded ¥142 billion. Yamanouchi’s growth rates from 1955 to 1959 averaged 16.4 percent, while from 1960 to 1964, they had reached a phenomenal 29.3 percent.\footnote{The Fifty-Year History of Yamanouchi Pharmaceutical Company, 132-133.}

\textit{Implementing an In-House Research Organization for New Drug Development}

Thanks to over a decade of stable growth, achieved by introducing foreign technologies, Yamanouchi’s managers gradually began to shift the focus of their strategies from the manufacturing and marketing of existing products of foreign origin to the in-house development of new drugs. To aid in the transition, the managers decided to construct a central research facility in Azusawa, Tokyo. The facility was to be
headed by Doctor Masao Murakami, a specialist in the development of synthetic chemical drugs, who was recruited directly from Osaka Industrial Science Research Center (Osaka Sangyō Kagaku Kenkyūsho) in 1962.

According to a 7 December 2000 interview with Yōshi Kobayashi, who spoke with former president, Shigeo Morioka, on the writer's behalf, Kenji Yamanouchi played an important role in recruiting Murakami and thus in bringing about the company's transition toward becoming a more research-based pharmaceutical enterprise. Morioka, who had worked closely with Kenji Yamanouchi, stated that without the founder's qualities both as a person and entrepreneur, a scientist of Murakami's caliber would never have considered leaving his prestigious research post to join what was then still a relatively small pharmaceutical manufacturer.44

It was also clear from a 6 April 2001 interview with Kunio Watanabe, a former senior manager at Yamanouchi, that hiring Murakami marked a major turning point in the company's drug development strategies. Murakami, who headed the basic research and drug investigation department of the central research laboratory, was recruited in hopes of strengthening the company's overall research capabilities. Based on Watanabe's assessment, it would not be an exaggeration to say that Murakami influenced the company's drug development focus until the early-1990s when another major shift was made toward biotechnology.45

Under Murakami's direction, managers went about improving the company's research capabilities by adopting a different approach from most other pharmaceutical manufacturers. While most firms hired competent staff prior to constructing a research facility, in Yamanouchi's case, the facility came first.46 It was only after the facility, a central laboratory, had been erected that Murakami began to train the new staff in drug development based on synthetic chemistry, the first of which

44. Yōshi Kobayashi, interview with Shigeo Morioka on the writer's behalf, 7 December 2000.
45. Kunio Watanabe, interview, 6 April 2001. This trend would continue until 1992 when Terahisa Noguchi, was appointed as head of Yamanouchi's biotechnology research activities.
46. Arakawa, 75.
was vitamins.

Murakami possessed the ability to identify researchers' weaknesses in certain scientific disciplines, devise specific measures to remedy them, while also pursuing his goal of developing novel products. He skillfully dealt with their lack of scientific and technical expertise by introducing a strategy of *learning by imitating*. In this way, researchers acquired the fundamental knowledge and techniques to produce important drugs in the laboratory that had already been launched by foreign pharmaceutical manufacturers.\(^47\) Once they had successfully mastered the processes by which the drug in question had been developed, they were then able to produce it by means of a different method, which could be patented according to the legislation in place at that time. The long-term objective of this strategy, however, was not simply to imitate but rather *to learn how to innovate*. In later years, researchers were able to make truly novel changes so as to enhance a drug's efficacy or reduce side effects.\(^48\) Thus, even a drug that was not first or second to market could become the preferred treatment, one example being Gaster (Pepcid in the United States).

**Drug Launches**

In an age when developing innovative drugs requires the application of a combination of different, often highly sophisticated technologies it is difficult to imagine that vitamins were once considered major medical breakthroughs. However, discovering their existence, isolating them, exploring the ways that they function in the body to prevent or cure diseases while also employing the latest methods to mass-produce them (making importation unnecessary) were all significant steps in the historical development of the Japanese pharmaceutical industry and catalysts for growth. Yamanouchi's three launches were Caromide (B\(_{12}\)), Cometamin (B\(_1\)) (both marketed in 1967) and Pyromijin (B\(_6\)) (1969).

Under Murakami's guidance, researchers were able to develop alternative methods to produce these substances; however, they were not the first to launch them. In those days, vitamins were one of the most

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47. Kunio Watanabe, interview, 6 April 2001.
48. This is true of Gaster, an H\(_2\) blocker, which offers novel improvements (reduced side effects) over the existing the remedies.
competitive drug categories, and by the time that Yamanouchi had launched its vitamin B products, others were already marketing similar ones. Takeda, still Japan’s largest pharmaceutical manufacturer, had already launched a vitamin B₃ product and filed a lawsuit against Yamanouchi in 1966, ending in an out-of-court settlement two years later. It may be for this reason that some in the industry once mockingly referred to Yamanouchi as Mane-no-Uchi (Yamanouchi, the imitator).

On the other hand, not all of Yamanouchi’s products sparked as much controversy; moreover, some showed real novelty. Yamanouchi’s laboratory was the first to develop a synthetic chemical process for producing glutamine, originally discovered by British scientist, Frederick Hopkins in 1921, according to a biochemical method. Thus, Yamanouchi’s researchers not only succeeded in developing a novel technique, but were also able to mass-produce their product (not feasible according to Hopkins’s method), a discovery that caught the attention of the scientific community.⁴⁹ Yamanouchi’s research team called it Tathion, which became the first tangible result of Murakami’s efforts and evidence that the company was gradually moving toward becoming a more innovative enterprise.

EFFECTS OF THE REGULATORY ENVIRONMENT ON CORPORATE STRATEGIES

(A) Safety in Manufacturing (GMP)

The stricter manufacturing regulations of the 1970s came in the wake of a series of drug-related incidents, the most famous being Thalidomide. Consequently, in 1969, the World Health Organization approved stricter safety regulations, later known as Good Manufacturing Practices (GMP), to which there were some 130 signatories, including Japan. The internationally agreed upon practices were implemented into domestic legislation in 1976, first as JGMP (Japanese Good Manufacturing Practices); then in 1979, they became the Pharmaceutical Affairs Law and were put into force in September 1980.

Although Yamanouchi was not directly implicated in the safety-

related incidents of the 1960s, the new legislation that followed was to have a profound effect on its operations as well as those of all Japanese pharmaceutical manufacturers. First, the adoption of manufacturing standards signified a considerable investment in new plant facilities. Yamanouchi's factory buildings, many of which were still wooden structures, were demolished, replaced with metal facilities and furnished with new, upgraded equipment. Also, because of the possibility of contamination as well as human error occurring at the time of packaging or shipping, standardized procedures were implemented at virtually every level of the pharmaceutical manufacturing process from the building specifications and ventilation equipment to the labeling and coding of products for delivery.

The process of becoming a modern manufacturer in every sense of the word began in the early 1970s, reaching fruition in the 1980s when Yamanouchi received approval to export products manufactured at its factories directly to the United States. At that time, inspectors from the American Food and Drug Administration (FDA) made visits to the Yaizu plant to verify that Yamanouchi's facilities met international standards. According to a 17 April 2005 correspondence with Yôshi Kobayashi, Yamanouchi was one of the leaders in the implementation of the latest GMP standards. Moreover, researchers at the Yaizu factory kept themselves abreast of any changes at the FDA so as to be prepared for further modifications in safety standards. Some measures that Yamanouchi implemented were the use of robots and other forms of mechanization to ensure a completely bacteria-free environment and the installation of special sterilization equipment to prevent contamination. Yamanouchi was even named a "model case," and observers who visited the Yaizu facility could view part of the production process through a glass window as they walked down the factory corridors.50

The upgrading of Yamanouchi's factories was a major preoccupation of management throughout the 1970s. Although the process was costly and time-consuming, it was a necessary phase in the historical development of the industry as a whole. Just as in the 1950s when new

technologies for mass-production were introduced to dramatically increase the speed and volume of production, these new regulations fundamentally improved the level of quality, while also raising employees' level of consciousness regarding the importance of safety.

From an industrial history perspective, the implementation of international standards was significant. Because they were international, it meant that the products manufactured at Japanese factories were of identical quality to those produced in other developed nations. Though internationalization would not be declared an official corporate strategy at Yamanouchi until the mid-1970s, the fact that it was among the first Japanese pharmaceutical manufacturers to adopt the international standards clearly indicates a strong interest in overseas development.

(B) Changes in the Regulatory Environment and their Effects on Innovation

In the introduction, mention was made of some of the early policies that helped to foster the emergence and development of the Japanese pharmaceutical industry. However, it should be added that regulations, or regulatory policy, also shaped the development pattern of the Japanese pharmaceutical industry. Temin wrote: "the present drug market is not simply a product of technical progress in the last generation. In fact, the opposite is more nearly true: many characteristics of the drug industry are products of our view of drugs and of the regulations imposed on their use..." Indeed, changes in the regulatory environment have had a direct impact on managers' formulation of strategies and served as one of the key factors in the shift in focus from manufacturing/marketing to research-based drug development.

The most significant reforms of the 1970s were: (a) the patent reform of 1976, (b) the banning of the sale of free samples (tempu hanbai) in 1978; (c) the full liberalization of capital in 1975; (d) the first prescription practice reforms (iryō bungyō gannen) in 1974; (e) the listing of drugs by their brand names (meigarabetsu yakkakijun kokuji)

in 1977 and (f) the implementation of Good Post-Marketing Surveillance Practices (GPMSP) in 1979. All of the legislation cited above had a marked effect on the strategies of all Japanese pharmaceutical manufacturers and contributed to corporate innovation; however, there are two which are of particular interest in this study.

(i) Patent Reform

The primary catalyst for innovation in the Japanese pharmaceutical industry was the patent reform, the effects of which are illustrated by the rise in the number of patent applications after 1976.

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Japanese Applications</th>
<th>Number of Foreign Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1975</td>
<td>2,157</td>
<td>735</td>
</tr>
<tr>
<td>1976</td>
<td>2,585</td>
<td>922</td>
</tr>
<tr>
<td>1977</td>
<td>2,810</td>
<td>940</td>
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<tr>
<td>1978</td>
<td>3,180</td>
<td>1,012</td>
</tr>
<tr>
<td>1979</td>
<td>3,651</td>
<td>985</td>
</tr>
</tbody>
</table>


While the patent reform was not actually put into force until 1976, there was already speculation at Yamanouchi as early as 1968 that a change would be forthcoming.52 Evidence that Yamanouchi’s managers anticipated a reform and had set about improving research capabilities is revealed in the 1970 launch of Josamycin, a macrolide antibiotic. Josamycin became Yamanouchi’s first international product, a clear sign that a strategy of drug development based on innovation was in place. This product was first licensed to DuPont in the United States, then to a

52. Arakawa, 90. In addition, two surveys of the Japanese pharmaceutical industry reveal the change of opinion. Tateo Kobayashi, “Tokkyōhyō no Ichibu wo Kaisei suru Hōritsu ni tsuite (jō)” (Patent Law Reform, Part One), Jurist, No. 595, 1 September 1975, 60. In 1955, 55.2 percent of the pharmaceutical companies surveyed were opposed to the recognition of product patents, while only 30.2 percent were in favor. When the Japan Patent Association carried out the same survey in 1970, the opposite was true; 70.6 percent were in favor of implementation. These results indicate that the managers had begun to endorse the implementation of a system to protect the fruits of their research.
number of European firms including Rhone-Poulenc in France, where it became the top selling antibiotic in 1984. Perdipine, a calcium antagonist, whose development began around the time of the patent legislation reform, was launched in 1981 and became the fourth best-selling drug in Japan in 1987.

(ii) The Banning of Free Samples

Prior to the 1978 ban, physicians were able to prescribe and dispense free samples or tempu hanbai, provided in large qualities by the manufacturers, for which they were able to receive NHI reimbursement. According to an interview with Yōshi Kobayashi on 17 April 2005, the banning of free samples had a marked effect not only on Yamanouchi’s operations but also on virtually all Japanese pharmaceutical manufacturers. Before the ban, medical institutions would make large purchases of their products in exchange for free samples. Kobayashi added that given the choice, most physicians would have preferred to prescribe the most innovative products marketed by the largest pharmaceutical manufacturing companies. Nonetheless, they continued to dispense less innovative products until the ban.53

After the reform, Yamanouchi could no longer offer these incentive to physicians, a situation that necessitated a major change in corporate strategies. According to Kunio Watanabe, a senior manager, interviewed on 6 April 2001, across the industry, corporate operations were so keenly affected by the change that many referred to it as the tempu shock.54 Consequently, after 1978, firms were left with no other choice but to improve their product lines by increasing investment in research.

The tendency to invest more heavily in research after the banning of free samples can be considered a common feature among all pharmaceutical manufacturers, as antibiotics, which most firms sold, were the most popular sample offered. With the implementation of new legislation, a new purchasing pattern also emerged: physicians, especially at large medical institutions, began to request a top-three product, since they were more innovative and provided a higher drug

reimbursement.55

CONCLUSION

This study investigated the key factors in the transition of a representative pharmaceutical company from manufacturer and marketer of existing drugs to the earliest phase of its emergence as an innovator. As seen through numerous examples, the development process was not smooth, which forced entrepreneurs/managers to constantly reassess corporate strategies so as to devise new ways to compensate for weaknesses. In this way, they continued to adapt to the changes in healthcare policies and regulations, while also taking advantage of scientific and technological breakthroughs.

Throughout the period in question, two entrepreneurs in particular, Kenji Yamanouchi and Junpei Watanabe, were of vital importance to corporate development as they provided a guiding managerial philosophy for employees over the long-term. Masao Murakami’s guidance also contributed to innovation at the company. His approach gave the company’s research activities a clearer long-term vision, thus elevating it to a higher status among corporate strategies. In his role as an educator, he aided in the improvement of the overall level of researchers’ technical and scientific skills by providing them with the foundation upon which to begin—though gradually—to pursue genuine novelty, rather than mere imitation. Such figures were of vital importance to Yamanouchi’s corporate history; however, there were undoubtedly other highly adept and perspicacious Japanese pharmaceutical industry leaders with a similar vision of improving their enterprise’s capabilities for innovation.

Finally, it was shown that government also played a significant role in the origins of innovation in the Japanese pharmaceutical industry, first by implementing global manufacturing standards (GMP) and later by patent reform. The change in the patent legislation effectively served to define the course of pharmaceutical industry development from the mid-1970s to the present-day. As a result, Japan would follow the

55. For a historical overview and analysis of the drug pricing system, the reader may refer to the following. Yongue, 82-86.
growth pattern of advanced western nations, rather than continue to foster the type of imitation industry that one finds in some developing nations with limited patent protection. The most important consequence of the patent reform of 1976 was that it simply gave Yamanouchi and its competitors no other choice but to reduce their reliance on foreign technologies and to undertake in-house research. Accordingly, from the mid-1970s, some pharmaceutical manufacturers were able to develop and launch a small number of products, whose novelty made international marketing (in western nations) through licensees an achievable goal.

This study has provided an analysis of the main factors in the origins of innovation in the Japanese pharmaceutical industry. However, because 1976 was only the starting point, one could not yet describe the Japanese pharmaceutical manufacturers of the late-1970s as truly innovative by international comparison. Yet, with the effects of growing investments in research and development made possible by the increasing demand for pharmaceuticals coupled with the constant readjustment of strategies in response to policy modifications, Yamanouchi and others like it were slowly able to build upon their nascent innovation capabilities. In this quest to further enhance corporate innovation, entrepreneurs would continue to play a decisive role.