Domestic Production of Anti-TB Drugs in Occupied Japan

— From the Historical Viewpoint of International Standards and Public Health —

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The purpose of this paper is to explore the reason why occupied Japan could halve tuberculosis (TB) mortality rate and improve its public health. Specifically, this paper examines the circumstances and history of the Japanese pharmaceutical industry, which attained to domestically produce higher-quality, larger-volume anti-TB drugs at a lower cost, with the intention of GHQ / SCAP / PHW. In 1945, Japan's public health seemed to be devastated. TB in Japan was called an exiled disease, and its mortality rate was the highest in the world. GHQ / SCAP PHW Chief Crawford F. Sams (Brigadier General) wanted the Japanese pharmaceutical industry to be self-sufficient without using United States aid. From the first in 1945, the U.S. military's intention to improve Japan's public health was to protect the health of its military personnel stationed in Japan and their families. Accepting the intention of PHW, the Japanese pharmaceutical industry used the SQC method that W. Edwards Deming introduced to Japan in 1950 for the production process of anti-TB drugs. The Japanese pharmaceutical industry drastically reduced the TB mortality rate by half in 1952 compared to 1947. The pharmaceutical industry contributed to the improvement of public health by domestically producing higher-quality anti-TB drugs in larger-volume. It provided those TB drugs to the Japanese market at lower prices.

Keyword: Occupied Japan (占領期), Anti-TB drugs（抗結核薬), Statistical quality control（統計的品質管理）

1. Introduction

(1) Historical Background

In 1945, public health in Japan was devastating. Notably, people called TB as a disease to ruin a national. The TB mortality rate was by far the highest in the world. GHQ/ SCAP/ PHW Chief Crawford F. Sams (Brigadier General) wanted the Japanese pharmaceutical industry to be self-sufficient in 1945 to produce good quality healthcare products by itself without any distribution or aid from the United States not spending the US national budget. (Sams, 1949) However, the U.S. military intended to improve Japan's public health to protect the health of the military personnel of its own country, who stationed in Japan with their families at that time.

With the intention of PHW, the Japanese pharmaceutical industry used the SQC method that Edwards Deming introduced in Japan in 1950 for the production process of anti-TB drugs. The Japanese pharmaceutical industry reduced the TB mortality rate of people by half. It contributed to improving public health in occupied Japan by domestically producing high-quality anti-tuberculosis drugs in larger volume and providing them to the Japanese market at lower prices.

This paper follows the themes of the paper issued in 2019 analyzing the intentions of the Public Health and Welfare (PHW) of GHQ, (Sato, 2019) and the paper issued in 2020 considering the reorganization of science and technology during Occupied Japan by GHQ/SCAP, (Sato, 2020) and developed the discussion in this paper.

The SQC, a measure to mass-production of high-quality pharmaceutical products inexpensively, was an essential technique for PHW, Ministry of Health and Welfare (MHW), and the pharmaceutical industry in Japan to reduce the mortality rate, which was the most critical issue of public health in Japan at the time.

The United States, which led the occupation, introduced the statistical quality control (SQC) having been used in the military field in the United States to the occupied Japan in 1950 to promote Japanese economy. The Japanese pharmaceutical industry which accepted the intention of GHQ / SCAP /PHW, wanted to promote its development. On the other hand, it desired to decrease the highest Japan's TB mortality rate in 1950.

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Since 1951 when approaching the end of the occupation, the United States changed its policy toward Japan. It intended Japan to expand military production for the United States after its severe financial and monetary contraction policy of Dodge Line in 1949 and Korean War in 1950. (Sugita, 1999)

Economic Science Section (ESS) of GHQ/SCAP appointed W. Edwards Deming to instruct the SQC to the Japanese pharmaceutical industry because ESS expected the pharmaceutical industry in Japan would produce a larger volume of higher-quality pharmaceutical products at a lower cost, and export them.

2. Previous Studies

First, this paper examines the previous research and tentatively answers the research question mentioned above.

Sams wanted the pharmaceutical industry in Japan to manufacture a more significant volume of higher quality pharmaceutical products at a more moderate price to reduce the mortality rate. Then, for PHW, MHW (Ministry of Health and Welfare in Japan), and the pharmaceutical industry in Japan, the SQC, advocated by Deming, was the method to produce a larger volume of higher-quality pharmaceutical products at lower-cost. (Sato, 2019)

SQC was one of the essential measures to reduce the mortality rate. For ESS, the SQC was the critical technique to lead Japan back to international society by exporting a large volume of high-quality products at low cost. (Sato, 2019)

The reorganization of science and technology in Occupied Japan by GHQ, including the perspective of public health quality control included the intention to transform Japan into a supply base that conformed to global standards for the world. (Sato, 2020)

Eiji Takemae states that the postwar healthcare reforms became one case of the most ideal implementation of human rights in the 20th century. (Takemae, 1986) Then, how were mortality and birth rates managed? According to *One Hundred Years' History of the Medical System,* the Ministry of Health and Welfare (Former Ministry of Health, Labor and Welfare) prepared public health statistics.

According to these statistics, until 1951 when the highest mortality rate changed from tuberculosis to brain hemorrhage, nearly 30 years since pneumonia or bronchitis changed from its first cause of death to the tuberculosis in Japan and the World in 1935. (Sams, 1949) (Koseishoimukyoku, 1976b)

Mikio Watanabe studies postwar healthcare history focusing on the BCG Disputes, which was the controversy occurred in 1951 over compulsory BCG vaccination, the Immunization Act, which regulated vaccination to prevent the outbreak and spread of potentially infectious diseases from a public health perspective, adopted in 1946, and the TB Control Act, which was the law to prevent TB infection, establish necessary medical measures for TB patients, and prevent new TB infections, passed in 1951. (Watanabe, 2009a)

Watanabe states that when reviewing the primary materials in Occupied Japan, he found a lot of historical facts that had predicted the occurrence of current health, medical care, and welfare problems. He insists that to study the establishment process of the legal system and its problems in the postwar period, solutions to such problems, and reception process of the people in Japan is required to solve the current comprehensive problems of health, medical care, and welfare.

From the viewpoint of healthcare history, Watanabe does research in the BCG Disputes, which occurred in 1951 at the end of the occupation period when the Immunization Law, which was said to be the most powerful system in the world was enacted. Moreover, the Government entirely revised the TB Control Act against the tuberculosis, which had been called a national disease in Japan. Watanabe points out the chemotherapy including streptomycin, which was imported to Japan from the United States in 1949, contributed to large reduction in the TB mortality rate in Japan. He also says that the establishment of the TB Control Act was, however, delayed in 1951. He refers to the results of TB survey conducted after the Commemoration Ceremony of Fifty Percent Reduction of TB Mortality Rate held in May 1952 showed that the TB mortality rate decreased, though the tuberculosis infection still widely spread in Japan. (Watanabe, 2009b)

As discussed in the BCG Disputes, BCG could neither prevent TB infection nor cure it. (Watanabe, 2009a) Therefore,

it was chemotherapy that contributed to the reduction in the tuberculosis mortality rate and the increase of efficacy for affected patients.

Akihito Suzuki says that PHW made effort to reduce the incidence of TB and venereal disease because both diseases were serious impediments to improving standards of public health in Occupied Japan. According to Suzuki, although the TB was the leading cause of mortality among Japanese until 1950, which had higher mortality rate than that of venereal disease, to protect the health of the American servicemen who consorted with Japanese prostitutes was more critical for PHW officials and Chief of PHW, Crawford F. Sams. Moreover, policies towards both TB and venereal disease did not emerge clearly until some years into the occupation, mainly because acute infectious diseases as smallpox, typhus and cholera were more urgent threats to public health in Occupied Japan.

PHW at last started to address TB in 1947. Those circumstances were found in the statements provided by Sams to the Allied Council for Japan (ACJ) in 1947. PHW and the Ministry of Health and Welfare in Japan devoted more energy and resources to controlling TB and venereal diseases by measures, such as tuberculin, X-rays and blood tests, immunization with BCG, and diagnostic works in laboratories. Health centers worked to grasp the scale of problems and control them. (Aldous, 2012)

Prominent previous studies have focused on the public sector. Then, how was the private sector working? This paper clarifies it. Specifically, this paper examines how the pharmaceutical industry contributed to public health.

3. Domestic Production of Anti-TB Drugs

This Chapter examines the domestic production of anti-TB drugs in Japan, especially streptomycin and PAS.

(1) Early History of TB and the Prevention Measures in Japan before 1945

Before explaining the production of anti-TB drugs, this section should describe the history of TB. TB has a long history in Japan. The ancient Japanese medical book, “Ishinho” was written in 984. It describes the symptoms of pulmonary TB. In 1805, Japanese citizens already knew that TB was an infectious disease and contagious through the media of various clothes, utensils, and other things used by TB patients. In April 1904, the Japanese government promulgated the first ordinances about the prevention of pulmonary TB. According to the regulation, the government provided spittoons in schools, factories, theaters, and other places designated by the local governors. Spitting other than in spittoons was prohibited. (U.S. Headquarters Army Service Forces, 1945)

Private organizations, including the Japanese White Cross Society for preventing disease, started in 1911, and the Japanese Association for the Prevention of TB established its foundation in 1915. The first national sanitorium began its operation for pulmonary TB patients. The government granted the subsidy to cities of more than 300,000 inhabitants for establishing good sanatoria for TB treatment. (U.S. Headquarters Army Service Forces, 1945)

The first TB statistical study started in 1899. From the statistical point of view, for the period 1915 to 1920, the average TB mortality rate was 231 of 100,000 people. The TB mortality rate was higher for females than it was for males.

In the early 1930s, Japan began industrial development. The government had to provide proper measures to prevent TB or treat TB patients all over Japan. The government ordered to establish sanatoria in the Prefectures of Osaka, Hyogo, Gunma, Chiba, Tochigi, Mie, Aichi, Gifu Yamagata, Fukui, Ishikawa, Okayama, Yamaguchi, Oita, and Kumamoto.

There were still many people who died in the above sanatoria. Japan needed to implement TB preventive measures or treatment to stop the high mortality rate. (U.S. Headquarters Army Service Forces, 1945)

(2) TB Prevention Measures in Japan during World War II

Japan Society for the Promotion of Science (JSPS) conducted joint research on BCG at the Tuberculosis Prevention Committee since September 1937. In 1943, the JSPS announced its research results. The Government of Japan expanded the scope of BCG vaccination from national school students to people provided under the National Physical

Fitness Law, including workers at factory establishments, students, pupils, and families of TB patients. The Government established the BCG vaccination manufacturing office in the TB Prevention Association. The national treasury subsidized the BCG vaccination fees of such people. The above measures led ten million people to receive the BCG vaccination in a year. In January 1944 Kekkaku Yobo Taisaku (Tuberculosis Prevention Measures) were decided in the Cabinet in Japan. (Koseishoimukyoku, 1976a)

(3) TB Prevention Measures in Occupied Japan

The government imported 200 grams of streptomycin for research activity in February 1949. Subsequently, in September 1949, the Cabinet decided on the outline for securing domestic production of streptomycin. The government allowed domestic production of streptomycin and PAS calcium in 1950. In the same year, the government covered streptomycin and PAS calcium for social insurance coverage. Since then, two anti-tuberculosis drugs have played a significant role in improving tuberculosis medicine. The TB mortality rate in Japan, however, was still in the highest position, namely 146.4 per 100,000 people, compared to other infectious disease mortality rates in 1950. (Koseishoimukyoku, 1976a)

(4) Production of Streptomycin

Streptomycin started being imported in 1949, and chemotherapy of the drug helped reduce TB mortality rate. (Watanabe, 2009b) The medical cure with streptomycin started in 1949 when 200 and 400 kilograms of that anti-TB drug was first imported in March and the next in October. This volume of streptomycin was only 1% of 60,000 kilograms, which Japanese would have annually needed. (Aldous, 2012) Japan needed to manufacture anti-tuberculosis drug domestically. The above 600 kilograms of streptomycin were positioned to instruct its usage to Japanese physicians and to create demands for that anti-TB drug in Japan.

GHQ/SCAP planned to create sufficient demands for streptomycin in Japan. GHQ/SCAP wanted Japanese manufacturers to produce streptomycin domestically and to commercialize such anti-TB drug in Japan. In the *PHW Weekly Bulletin* from October 14, 1945 to December 31, 1949 reproduced by Satoshi Sugita, 200 kilograms and 400 kilograms of streptomycin were distributed to the following pharmaceutical companies in Japan in July and October respectively, not to hospitals.

In July, the weekly bulletin shows the following distribution list: 53,197 grams to Takeda Yakuhin Kogyo K.K. (Takeda Pharma), 50,000 grams to Shionogi Seiyaku K.K. (Shionogi Pharma), 41,195 grams to Sanyo K.K. (Sanyo Pharma), 32,396 grams to Yamanouchi Seiyaku K.K. (Yamanouchi Pharma), the remaining grams to Banyu Seiyaku K.K. (Banyu Pharma). (Sugita, 2008)

In October, the weekly bulletin shows another distribution list as follows: 100,000 grams to Takeda Pharma,50,000 grams to Shionogi Pharma, 30,000 grams to Tanabe Pharma, 30,000 grams to Fujisawa Yakuhin Kogyo Co., Ltd. (Fujisawa Pharma), 30,000 grams to Yamanouchi Pharma, 30,000 to Dainippon Seiyaku Co., Ltd.(Dainippon Pharma), 30,000 grams to Daiichi Seiyaku Co., Ltd. (Daiichi Pharma), 20,000 grams to Sankyo Pharma, 20,000 grams to Torii Seiyaku Co., Ltd.(Torii Pharma), 20,000 grams to Tokyo Tanabe Seiyaku Co., Ltd.(Tanabe Pharma, Tokyo), 20,000 grams to Banyu Pharma and 20,000 grams to Nakamura Taki Shoten Co., Ltd.(Nakamura Taki Pharma). (Sugita, 2008)

(5) Production of PAS

Japanese private companies started domestic production of streptomycin in July 1950. In 1952, large factories in Japan succeeded in producing necessary volumes of streptomycin. They also produced PAS as anti-TB drug, which was said to assist streptomycin. Reduction percentage in TB mortality rate increased from 1951 to 1953. The number of people infected with tuberculosis, however, was still high. The rate of TB infection in 1961 was 445.9 / 100,000 population (0.445%), which was still high after 10 years later in Japan. Since the infection rate of venereal disease followed the same process. Akihito Suzuki calls such nature of diseases with this phenomenon as "entrenched nature of chronic infection disease." (Aldous, 2012)

According to the Japanese Society for History of Pharmacy (JSHP), Tanabe Pharma, which has the oldest history in Japan, obtained the approval by MHW to domestically manufacture and sell PAS as anti-TB drug in May 1950. It was two months earlier the time when five Japanese companies including Meiji Seika obtained the approval to sell domestically produced streptomycin in July 1950. (Nihon Yakushi Gakkai, 1966)

Pharmaceutical companies in Japan declined to manufacture streptomycin by themselves at first, however, since they did not afford a large amount of facility investment and high level of technology for fermentation equipment. In July 1950, Meiji Seika Kaisha, Limited (Meiji), Kyowahakko Kogyo Co., Ltd (Kyowa Hakko), Kaken Kagaku Co., Ltd. (Kaken Kagaku), Shimane Kagaku Co., Ltd. (Shimane Kagaku), Nihon Seibutsu Kenkyujo Co., Ltd. (Nihon Seibutsu Kenkyujo) obtained the approval to manufacture and sell streptomycin in Japan. Streptomycin, however, decreased its administration since it caused hearing loss as a side reaction. (Nihon Yakushi Gakkai, 1966)

At the Headquarters of Tanabe Pharma in Osaka, after 1948, researching staff began to read the latest American healthcare books stored in the GHQ Library, which was located in Osaka City. At that time, Ikuhisa Nakamura, who was a manager of the Documents Department of Tanabe Pharma, found a paper entitled "The Treatment of Tuberculosis in Sweden with para-aminosalicylic acid (PAS): A Review" published on a pharmaceutical journal, "The Lancet" in 1946 by Swedish Scholar, Jorgen Lehmann. The chemical structure of PAS was similar to that of salicylic acid, which Tanabe Pharma had worked on salicylic acid for many years. Tanabe Pharma had imported salicylic acid from Germany since 1882 and had sold that chemical as antiseptic agent. Further in 1897, Tanabe Pharma started to manufacture salicylic acid by itself. Therefore, researchers and engineers were accustomed to devising synthesis methods and characteristics. (Oda, 2001)

Since August 1948, Tanabe Pharma, Tokyo had addressed in manufacturing PAS under the supervision of Dr. Shigehiko Sugasawa of Pharmaceutical Sciences, Tokyo University. Tanabe Pharma was successfully synthesized 500 grams of PAS prototype. (Tanabe, 1983) Whereas streptomycin was a case of anti-TB drug managed by PHW, PAS was a case of anti-TB drug developed independently by Tanabe Pharma with a paper of Jorgen Lehmann who discovered that PAS was available oral administration. In addition, Tanabe Pharm received the permission from MHW on the paid distribution for clinical trials to doctors in 1949. (Oda, 2001) Tanabe Pharma started the sales of PAS with permission to manufacture PAS by itself in May 1950. By the end of 1950, 24 pharmaceutical companies participated in the PAS production in Japan. (GHQ, 1995)

(6) Combined Treatment of Streptomycin and PAS

The National Sanatoria History Study Group stated that in the first report of the Streptomycin Research Council conducted in November 1949, administration of streptomycin was intramuscularly injected twice a day of one gram in total per day and discontinued its administration up to 40 grams in total. The treatment was a short-term therapy. Mycobacterium tuberculosis decreased by about 50 percent. According to a survey after finishing the treatment, 25 percent of patients died. (Koseisho Imukyoku Kokuritsuryoyojokanai & Kokuritsuryoyojoshi Kenkyukai, 1976)

Then, the experts found the combined treatment of streptomycin and PAS could prevent the streptomycin tolerance, and then, the healthcare physicians began the combined use of streptomycin and PAS for the TB treatment. (Shimao & Kekkakuyobokai, 2016) The Streptomycin Research Council began a combination therapy of streptomycin and PAS for the first time since January 1951. (Koseisho Imukyoku Kokuritsuryoyojokanai & Kokuritsuryoyojoshi Kenkyukai, 1976)

(7) Who Controlled the Quality of Private Basis Pharmaceutical Products?

Penicillin and streptomycin were manufactured by protection, technical guidance, and assistance of GHQ, but PAS was greatly different from the above drugs because the technology of PAS was introduced on a private basis. (Nihon

Yakushi Gakkai, 1966) The high reduction in TB mortality rate already started from 1950, before the Tuberculosis Control Act was enacted. As mentioned above, considering the BCG vaccination did not contribute to the reduction in TB mortality rate, the outcome of chemotherapy at that time should not be ignored. The time of commercialization and release of PAS was earlier than those of streptomycin by two months in Japan.

The domestic manufacturing of PAS was approved in May 1950, and that of streptomycin was in July 1950. Three years after completion of the new facility of manufacturing streptomycin, the Meiji Seika received the grant of corporate tax exemption and was able to promote the project of manufacturing streptomycin. In addition, the government purchased manufactured streptomycin from July 18, 1950 to the end of 1951. (Meiji Seika Kabushiki Kaisha, 1987)

According to GHQ, the total volume of manufactured streptomycin in 1950 reached 118,600 kilograms. On the other hand, the total volume of manufactured PAS increased from 565 kilograms in January 1950 to 141,232 kilograms in total in 1950. (GHQ, 1995)

In November 1948, about a year before the introduction of anti-TB streptomycin to Japan in 1949, the serious death accidents occurred caused by a biological drug. In Kyoto prefecture, out of 7642 vaccinated people in total, 606 people suffered from toxic poisoning and 68 people died after the diphtheria vaccination. In Shimane prefecture, 15 of 322 vaccinated people died. In the Conference of Inspectors of Biological Preparations held on December 6, 1948, Sams strongly demanded the quality solution of pharmaceutical products by warning that the Preventive Vaccination Law in Japan was the best preventive vaccination law in the world, however, the death accidents of children caused by cheap and bad quality products manufactured by Japanese companies were disgraceful accidents for Japanese society.

From the time of 1948 the PHW required the need for quality control in the pharmaceutical industry. (Watanabe, 2009c) As mentioned in his book, *Medic*, Sams was particularly aware of importance of quality control and wanted Japanese pharmaceutical industry to be independent with establishment of high-quality standards and appropriate quantity of importing finished products. (Sams, 1998)

4. Transition of TB Mortality Rate in Occupied Japan and the World

To clarify the transition of TB mortality rate in Occupied Japan and the World, the chapter quotes the chart and the figure from the previous work of the Author as follows:

Chart - 1 Transition of TB Mortality Rate in the World

(per 1000,000)

	USA	Mexico	Hong Kong	Japan	Ryukyu Islands	Finland	Italy	England
1945	40.1	55.1		280.3		187	91	56
1946	36.4	55.2	109.5	261.2		178	84	53
1947	33.4	50.9	106.3	187.2		166.6	77.2	54.7
1948	30.2	47.9	108.9	179.9	65.7	155.5	61.5	50.6
1949	26.3	43.8	140.6	168.9	61	129.9	49.5	45.9
1950	22.5	41.1	145.9	146.4	66.3	93.6	42.6	36.3
1951	20.1	41.6	207.9	110.3	73	83.8	42.6	31.6
1952	15.8	36.2	168.1	82.2	78	57.7	27.7	24.1
1953	12.3	29.9	131.1	66.5	56.6	44.6	23.6	20.2
1954	10.2	27.1	121.6	62.4	48.7	40.4	23	17.8
1955	9.2	25.3	112.6	52.3	37.5	41.8	22.7	14.6
	USA	Mexico	Hong Kong	Japan	Ryukyu Islands	Finland	Italy	England
(1)	17.03%	13.22%	0.50%	31.10%	・・・	12.60%	26.70%	4.50%
(2)	29.00%	11.00%	-15.20%	43.80%	-17.60%	38.35%	34.97%	33.60%

(Sato, 2014)
(1): Percent decrease of TB mortality rate from 1946 to 1948
(2): Percent decrease of TB mortality rate from 1950 to 1952

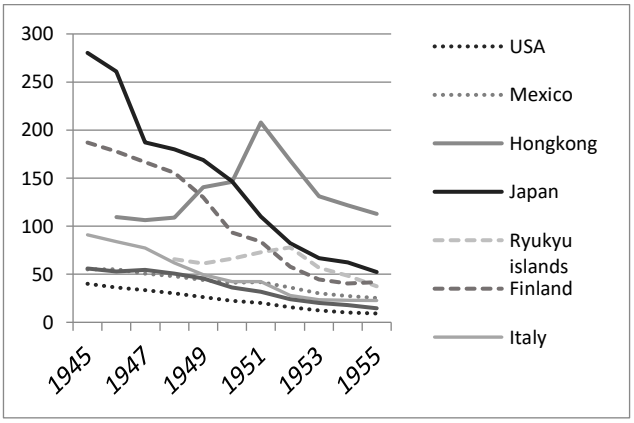

Figure - 1 Transition of TB Mortality Rate in the World
(Sato, 2014)

The reduction of Japanese TB mortality rate which is 43.80 % from 1950 to 1952 is higher than that of other countries or other three-year periods. (See (1) and (2))

The highest reduction rate of TB mortality by 43.8% from 1950 to 1952 in Occupied Japan attributes to the following possible reasons:

(i) To build public health center on a national basis. (Related to the public sector)
(ii) To start school lunch system. (Related to the public sector)
(iii) To start domestic production of anti-TB drugs. (Related to the private sector)

About (i), the Government enacted the Public Health Center Law in 1947, accepting SCAPIN 48 which stipulates the public health in Japan. Then public health centers affected since 1947. The reduction of TB mortality rate is related to the period from 1947 to 1949, namely the reduction from 187.2 to 168.9, which means 9.7% reduction.

Next, considering (ii), the nationwide school lunch system started on February 1951. (Zenkokugakkokyushoku Rengokai, 2019) Then, the period on reduction of TB mortality rate is from 1951 to 1953 following the above. The reduction number of percentages is 39.7%.

The third, as Chart 1 described (iii), domestic production of anti-TB drugs started in 1950. The reduction percentage of TB mortality rate is 43.8%.

Considering the correlation of TB mortality rate and prevention movement against TB, the domestic production of anti-TB drugs has the highest percentage of correlation.

5. Conclusion

This paper aims to explore why occupied Japan was able to halve the tuberculosis (TB) mortality rate and improve public health.

This paper followed the trends of the Japanese pharmaceutical industry, which produced higher-quality and larger-volume anti-TB drugs at a lower cost, with the intention of the Public Health Welfare Section (PHW) of General Headquarters Supreme Commander for the Allied Powers (GHQ/SCAP).

The Japanese pharmaceutical industry, especially pharmaceutical companies, by accepting the intention of GHQ/SCAP, made efforts to improve public health using statistical quality control method instructed by W, Edwards Deming during the occupation period.

The critical points of contribution of pharmaceutical companies contributed to Japanese public health in Occupied Japan are as follows:

(i) Domestic production of larger volume of higher quality anti-TB drugs at lower prices
(ii) Drastic reduction of high TB mortality rate during the period from 1950 to 1952

The Japanese pharmaceutical companies obtained the approval to domestically manufacture anti-TB drugs including streptomycin and PAS since 1950. They have been combined to dose the TB patients since 1951.

Furthermore, thanks to the SQC method advocated by Deming, the larger volume of high-quality anti-TB drugs at lower cost came on to the market. These anti-TB drugs met the SQC method which was considered as international standards in Occupied Japan. The Japanese Pharmaceutical industry in Occupied Japan realized the GHQ expectation to produce high-quality pharmaceutical products and reduce high TB mortality rate. Such a large volume of high-quality pharmaceutical products at lower cost connected to lead Japan back to international society.

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