

1, November 1947

*Supply, Prefecture*

TO : Commanding Officer  
Ehime Military Government Team APO 317  
Matsuyama Shikoku

SUBJECT: Explanation of the Penicillin Research Work.

FROM : Niihama Works of the  
Nissin Chemical Co., Ltd.

Dear Sirs:

We are extremely sorry for our insufficient explanation concerning the penicillin research of our company on the occasion of Doctor Hammlin's investigation of our Penicillin Research Section which, we admit, was not complete nor to the point. It was due to the absence of the chief of this section who was at that time, out on an urgent business trip to Tokyo.

In order to supplement the answers given on that occasion, we hereby submit a detailed report covering the whole data of the penicillin production. The annexed reports and data, we are sure, will give an accurate and concrete layout of our current penicillin research. But we will always be ready to answer any questions that is not fully answered or not covered in this report.

Yours respectfully,

*Y. Harada*  
\_\_\_\_\_  
( Y. Harada )

Director of the

Niihama Works

Nissin Chemical Co., Ltd.



### 1. Explanation

We are very sorry the explanation on the occasion of Mr. Hammlin's investigation was not satisfactory. The Chief of the Penicillin Research Section was absent on business trip and the man next in charge was absent on account of illness. With the his return we prepared the following report answering to the questions that was asked on that occasion.

### 2. Object of the current penicillin research.

With the purpose to execute research work on the culturing and refining processes and also to train the technical employees and their assistants in penicillin preparing processes, the now existing facility was constructed.

As is clearly described in the table (ANNEX 1) the facilities have not been worked at their full capacity from the start, i.e. the volume of the charge and time of charge per week was increased gradually in step by step.

The substantial production of commercial penicillin will not be carried out by the surface (bottle) culture process (for instance we utilized the Erlenmeyer flask that the company had on hand rather than purchase flasks that are more suited to utilize the space more efficiently) it is to be by the tank (submerge) culture process the construction of which has met with the approval of GHQ, SCAP and the Ministry of Finance. The construction of the penicillin plant is now under progress.

Recently, in order to meet the earnest demand of the Ministry of Health and also urged by our spontaneous desire to contribute as



much as possible to the health and welfare of the people, we decided to operate to the limit of our current facilities, and so have planned and endeavoured to increase the volume of charge to 100 liters and operate daily.

Consequently we have set our production goal for the month of November at 1,000 ampules (vials) of 30,000 units content, at the minimum.

3. Re: Penicillin yield.

(A) The yield of the penicillin produced in our plant was not always satisfactory. The principal reasons for this can be attributed to the facts firstly that it was the training period for the technicians and workers, and secondly that the facilities were not completed and arranged as desired. To be exact, the lack of the refrigerator for the rapid cooling of the cultured broth, the lack of filter-press for rapid filtration of broth, the lack of the super-cooling refrigerator for the freeze-drying process resulted in longer time requirement for the drying and difficulties even in maintaining the "final rich water" in a frozen state, (the later case was temporarily remedied recently by the utilization of dry ice), the inoperable state of the vacuum pump of the freeze-drying process, lack of measuring apparatus for the high vacuum.

Recently, these bottlenecks were almost completely solved. The increasing tendency of the yield can be attributed to this fact. At present are executing all efforts to raise the yield through the improvement of our processing technique.



(B) In discussing the yield of the penicillin process or any other products, the assay method will pose the most important problem. In this company, the dilution assay method was adopted together with the cylinder (cup) method. It is a well-known fact that errors are apt to rise by the dilution method. Meanwhile without a reliable standard penicillin assay by the cup method will not give accurate results.

However, as we could not be shared a standard penicillin from the Sanitary Research Institute of the Ministry of Health, were obliged to use our product penicillin as the working standard.

The sample submitted to the Sanitary Research Institute of the Ministry of Health for preliminary assay test gave following results.

|   |       |              |
|---|-------|--------------|
| Assay by dilution method<br>(In our assay room) | ----- | 300 units/mg |
|---|-------|--------------|

|  |       |               |
|--|-------|---------------|
| Assay by cup method<br>(Sanitary Research Institute) | ----- | 97.8 units/mg |
|--|-------|---------------|

Consequently by multiplying 0.33 to the results obtained in our assay room it may be said that one can arrive to the correct potency. However, as to be strict and to be safe, the multiplying factor of 0.25 instead of 0.33 was taken temporarily until we are able to ascertain by accurate assay with the standard penicillin.

(C) The figures for units on the table (ANNEX 1 and ANNEX 2) for after 30 Sept. and those in parenthesis up to Sept. 25 are the results obtained by multiplying 0.25 to the results obtained by the dilution assay method. As explained in paragraph 2 (b) the



multiplication of 0.25 is rather severe, hence on table (ANNEX 2) is set forth for reference the yields calculated by using 0.33 as factor.

Viewing the production program of the penicillin producing companies of Japan from November to December of this year (from reports submitted to Ministry of Health) the volume of broth required for the production of one ampule (30,000 units content) of penicillin is from 0.6 to 5 liters.

(Remarks: by the surface culture method). A certain number of these companies are using *Penicillium chrysogenum* (Q. 176) and obtaining 300 units per cubic centimeters hence the volume of broth required for one ampule (of 30,000 units) would be small. However, other companies are using the *Penicillium notatum* (NRRL 1978 and B.2) and other strains which give broths considerably lower potency, consequently the volume of the broth required for one ampule (of 30,000 units) would be large. Taking these facts into consideration, the 2 to 4 liters of broth required for one ampule of penicillin as is <sup>the</sup> case in our company cannot necessarily be regarded as bad. Every efforts have been and are being exerted to suspend the use of *Penicillium notatum* (B.2) and shift to *Penicillium chrysogenum* (Q.176).

(D) Although the average broth potency for the month of October was 35 units per cubic centimeters, the culture of one charge was finished in 5 days compared to the 9 or to 12 days required in other companies. Taking this condition into consideration the potency of the broth may be estimated at 70 units <sup>equivalent in</sup> ~~per cubic~~



~~centimeters~~  
*certain unit period.*

- (E) As formerly explained in this report we were not shared the standard penicillin for assay standard which caused us much inconveniency in checking the reaction in the cultivation refining and other processes because of the lack of accurate potency assay. By negotiation with the Ministry of Health and the Japanese Penicillin Research Association it was arranged that we be shared standard penicillin for assay use. (Expected to arrive on 6th of November)

4. Re: Raw materials.

(a) Pepton

Pepton is not being used at present, but in consequence of the favorable results obtained by addition of this substance even to the United States synthetic media, we have decided on its use before long. Estimated monthly consumption by the later on with the commencement of the operation of the penicillin plant by the tank (submerge) culture method will increase to 250 to 500 kilograms. (for only surface method 50 - 100 kgs.)

(b) Butyl-acetate

The current consumption of butyl-acetate is small as we are now refining the penicillin by utilizing active carbon but in the event we could acquire a sufficient supply are of the desire to shift to the direct extraction by butyl-acetate.

(c) Lactose

Experiencing difficulties in obtaining.



5. Re: Equipments.

The various shortcomings pointed out by Doctor Hammlin will be immediately remedied with gratitude.

6. Re: Disposition of the finished products.

As we had not received the legal assay tests (such as of its sterility, toxicity, pyrogens and etc.) of the Sanitary Research Institute of the Ministry of Health, we have strictly refrained in using it on human bodies.

Before long the toxicity test and pyrogens test will be entrusted to the Microbiological Research Institute of the Osaka University. All the penicillin products, outside of the assay sample used as mentioned in paragraph 2(b) and also those used for the working standards for the cup method and samples used for checking the refining process, are stored safely in our hands as the table (ANNEX 3) shows.



ANNEX 3

C O P Y  
of  
RECEIPT BOOK

1, Nov. 1947

Nissin Chemical Co., Ltd.

| Date received   | Units received    | Date Prepared | Units withdrawn | Date Prepared | Units on hand        |
|-----------------|-------------------|---------------|-----------------|---------------|----------------------|
|                 |                   | ) Total       |                 |               | 64,500 ( 16,125)     |
| (1) ( (Ca-salt) | 64,500 ( 16,125)  | ) units up    |                 |               |                      |
|                 |                   | ) to June.    |                 |               | 170,500 ( 42,625)    |
| ( (Na-salt)     | 106,000 ( 26,500) | ) 26          |                 |               |                      |
| June 27         | 216,000 ( 54,000) | June 27       |                 |               | 386,500 ( 96,625)    |
| July 1          | 456,000 (114,000) | July 1        |                 |               | 842,500 ( 210,625)   |
|                 |                   | 3             |                 |               | 964,100 ( 241,025)   |
|                 |                   | 7             |                 |               | 1,250,100 ( 312,525) |
|                 |                   | 18            |                 |               | 1,634,100 ( 408,525) |
|                 |                   | 21            |                 |               | 1,841,100 ( 460,275) |
|                 |                   | 24            |                 |               | 2,031,100 ( 507,775) |
|                 |                   | 27            |                 |               | 2,262,100 ( 565,525) |
|                 |                   | 30            |                 |               | 2,529,100 ( 632,275) |
| Aug. 3          | 359,000 ( 89,750) | Aug. 3        |                 |               | 2,888,100 ( 722,025) |
|                 |                   | 8             |                 |               | 3,170,100 ( 792,525) |
|                 |                   | 12            |                 |               | 3,423,100 ( 855,775) |



| Date received | Units received    | Date Prepared | Units withdrawn | Date Prepared | Units on hand         |
|---------------|-------------------|---------------|-----------------|---------------|-----------------------|
| Aug. 15       | 153,000 ( 38,250) | Aug. 15       |                 |               | 3,576,100 ( 894,025)  |
| 19            | 77,200 ( 19,300)  | 19            |                 |               | 3,653,300 ( 913,325)  |
| 22            | 373,000 ( 93,250) | 22            |                 |               | 4,026,300 (1,006,575) |
| 25            | 193,000 ( 48,250) | 25            |                 |               | 4,219,300 (1,054,825) |
| 29            | 323,000 ( 80,750) | 29            |                 |               | 4,542,300 (1,135,575) |
| Sept. 3       | 119,000 ( 29,750) | Sept. 3       |                 |               | 4,661,300 (1,165,325) |
| 5             | 199,000 ( 49,750) | 5             |                 |               | 4,860,300 (1,215,075) |
| 14            | 585,000 (146,250) | 14            |                 |               | 5,445,300 (1,361,325) |
| 22            | 585,000 (146,250) | 22            |                 |               | 6,030,300 (1,507,575) |
| 23            | 53,020 ( 13,255)  | 23            |                 |               | 6,083,320 (1,520,830) |
| 25            | 17,200 ( 4,300)   | 25            |                 |               | 6,100,520 (1,525,130) |
| 30            | 44,300            | 30            |                 |               | 6,144,820 (1,569,430) |
| Oct. 1        | 19,100            | Oct. 1        |                 |               | 6,163,920 (1,588,530) |
| 2             | 4,820             | 2             |                 |               | 6,168,700 (1,593,350) |
| 3             | 19,500            | 3             |                 |               | 6,188,240 (1,612,850) |
| 5             | 136,700           | 5             |                 |               | 6,324,940 (1,749,550) |
| 6             | 237,000           | 6             |                 |               | 6,571,940 (1,986,550) |



| Date received | Units received | Date Prepared | Units withdrawn      | Date Prepared | Units on hand  |
|---------------|----------------|---------------|----------------------|---------------|--|
| Oct. 7        | 41,700         | Oct. 7        |                      |               | 6,613,640 (2,028,250)  |
| 8             | 189,500        | 8             |                      |               | 6,803,140 (2,217,750)  |
| 9             |                |               | 373,000<br>(93,250)  | Aug. 22       | Supplied as sample for assay test to the Sanitary Research Institute, Ministry of Health, and also for working standard. |
|               |                |               | 216,000<br>(54,000)  | June 27       |  |
|               |                |               | 456,000<br>(114,000) | July 1        |  |
|               |                |               | 359,000<br>(89,750)  | Aug. 3        |  |
|               |                |               | 231,000<br>(57,750)  | July 27       |  |
|               |                |               | 267,000<br>(66,750)  | 30            |  |
|               |                |               | 282,000<br>(70,500)  | Aug. 8        | * As working standard.<br>3,619,140 (1,671,750)  |
| Oct. 10       | 42,000         | Oct. 10       | #                    |               | 3,661,140 (1,713,750)  |
| 11            |                |               | 189,500              | Oct. 8        | 3,471,640 (1,524,250)  |
| 13            | 202,000        | 10            |                      |               | 3,673,640 (1,726,250)  |
| 14            |                |               | 384,000              |               | As sample for experiments in the refining process.   |
|               |                |               | 585,000              |               |  |
|               |                |               | 136,000<br>237,000   |               |  |



| Date received | Units received | Date Prepared | Units withdrawn      | Date Prepared | Units on hand  |
|---------------|----------------|---------------|----------------------|---------------|--|
| Oct. 14       |                |               |                      |               | 2,331,640 ( 386,250)   |
| 19            | 243,000        | Oct. 19       |                      |               |  |
| 20            | 920,000        | 20            |                      |               |  |
| 21            | 158,000        | 21            |                      |               | 3,652,640 (1,707,250)  |
|               |                |               | 202,000              | Oct. 13       |  |
|               |                |               | 253,000<br>( 63,250) | Aug. 12       | For refining experi-<br>ments.<br>Vial broken. As display<br>sample. |
|               |                |               | 19,500               | Oct. 3        | 3,178,140 (1,422,500)  |
| 23            | 57,500         | 23            |                      |               | 3,235,640 (1,480,000)  |
| 24            | 41,500         | 24            |                      |               | 3,277,140 (1,521,500)  |
| 25            | 294,000        | 25            |                      |               | 3,571,140 (1,815,500)  |
| 26            | 157,000        | 26            |                      |               | 3,728,140 (1,972,500)  |
| 27            | 375,000        | 27            |                      |               | 4,103,140 (2,347,500)  |

Remarks: Figures in paranthesis shows the revised potency i.e.

(potency units prior to Sept. 30) X  $\frac{1}{4}$



## ANNEX 1

Laboratory Data  
of  
Penicillin Production

1, Nov. 1947

Nissin Chemical Co., Ltd.

| Expt. No. | Date of Refining | Culture charged (Liter) | Filtrated Culture for Refining |                      | Yield              |              | Potency * (Units/mg) | Remarks  |
|-----------|------------------|-------------------------|--------------------------------|----------------------|--------------------|--------------|----------------------|--|
|           |                  |                         | Volume (Liter)                 | Potency * (Units/cc) | (Units) *          | (Percentage) |                      |  |
| P - 10    | Feb. 12          | 9                       | 7                              | 20 ( 5)              | 24,000<br>( 6,000) | 17           | 113<br>( 28)         | *<br>Temporary assay results must be recalculated in comparison to standard by multiplying by 1/4. Correct units within parenthesis. Assay potency after Sept. 26 are correct. |
| P - 11    | 13               | 8.5                     | 7                              | 20 ( 5)              | 5,760<br>( 1,440)  | -            | 100<br>( 25)         |  |
| P - 12    | 19               | 6                       | 4                              | 30 (7.5)             | 25,000<br>( 6,250) | 21           | 254<br>(63.5)        |  |
| P - 13    | 25               | 9                       | 7                              | 50 (12.5)            | 43,200<br>(10,800) | 12.4         | 370<br>(92.5)        |  |
| P - 14    | 27               | 12.3                    | 3.5<br>(10)                    | 20 ( 4)              | 5,300<br>( 1,325)  | over 7.1     | over 57<br>(14.5)    |  |
| P - 15    | March 2          | 11                      | 8.5                            | 10 (2.5)             | 25,960<br>( 6,490) | over 30.5    | 407<br>(101.7)       |  |
| P - 16    | 7                | 13                      | 11                             | 20 ( 5)              | 52,000<br>(13,000) | over 23.6    | 122<br>(30.5)        |  |
| P - 17    | 10               | 13                      | 9.5                            | 20 ( 5)              | 83,500<br>(20,875) | 43.9         | 260<br>( 65 )        |  |



| Expt. No. | Date of Refining | Culture charged (Liter) | Filtrated Culture for Refining |   | Yield                |              | Potency* (Units/mg) | Remarks   |
|-----------|------------------|-------------------------|--------------------------------|---|----------------------|--------------|---------------------|---|
|           |                  |                         | Volume (Liter)                 | Potency* (Units/cc)                               | (Units)**            | (Percentage) |                     |   |
| P - 18    | March 12         | 13.3                    | 10                             | 20 ( 5)   | 60,000<br>(15,000)   | 30           | 315<br>(78.75)      | **<br>The charge was 10L, decrease to broken vessel |
| P - 19    | 16               | 13.3                    | 10.5                           | 20 ( 5)   | 20,000<br>( 5,000)   | 9.5          | 52.6<br>(13.15)     |   |
| P - 20    | 19               | 13.3                    | 10                             | 12 ( 3)   | 20,000<br>( 5,000)   | 25           | 105<br>(26.25)      |   |
| P - 21    | 21               | 22                      | 20                             | 16 ( 4)   | - ***                | -            | -                   | ***<br>Refining failure.                            |
| P - 22    |                  |                         |                                |   |                      |              |                     |   |
| P - 23    | 25               | 13.3                    | 9.5                            | 6 <sup>1</sup> -40(10)<br>35 <sup>1</sup> -60(15) | 160,000<br>( 40,000) | 35.5         | 465<br>(11.625)     |   |
| P - 24    | 27               | 13.3                    | 8.5                            | 10 (2.5)  | 13,600<br>( 3,400)   | 14.3         | 52.6<br>(13.15)     |   |
| P - 25    | 30               | 13                      | 9                              | 40 (10)   | 152,000<br>( 38,000) | 42.2         | 513.5<br>(128.375)  |   |
| P - 26    | April 8          | 20                      | 15                             | 40 (10)   | 160,000<br>( 40,000) | 26.6         | 243.9<br>( 60.975)  |   |
| P - 27    | 13               | 20                      | 15                             | 40 (10)   | 208,800<br>( 52,200) | 34.8         | 316.9<br>( 79.225)  |   |
| P - 28    | 17               | 19.750                  | 15                             | 40 (10)   | 210,000<br>( 52,500) | 35.0         | 317.4<br>( 79.35)   |   |
| P - 29    | 20               | 20                      | 15                             | 50 (12.5)   | 360,000<br>( 90,000) | 48.0         | 546.0<br>(136.5)    |   |
| P - 30    | 22               | 18.75                   | 15                             | 70 (17.5)   | 240,000<br>( 60,000) | 22.85        | 528.6<br>(132.15)   |   |



| Expt. No. | Date of Refining | Culture charged (Liter) | Filtrated Culture for Refining |                     | Yield                |              | Potency* (Units/mg) | Remarks   |
|-----------|------------------|-------------------------|--------------------------------|---------------------|----------------------|--------------|---------------------|---|
|           |                  |                         | Volume (Liter)                 | Potency* (Units/cc) | (Units)*             | (Percentage) |                     |   |
| P - 31    | April 25         | 20                      | 13                             | 32 ( 8)             | 104,000<br>(26,000)  | 25.0         | 235.2<br>( 58.8)    |   |
| P - 32    | 28               | 26                      | 15                             | 16 ( 4)             | -*****               | -            | -                   | ****<br>Experiment suspended due to trouble of pump.    |
| P - 33    | May 1            | 22.5                    | 9                              | 32 ( 8)             | 90,000<br>(22,500)   | 31.25        | 234.4<br>( 58.6)    |   |
| P - 34    | 9                | 25                      | 15                             | 0                   | *****                | -            | -                   | *****<br>Experiment stopped due to low culture potency. |
| P - 35    | 11               | 17                      | 12                             | 50(12.5)            | 348,000<br>(87,000)  | 38.0         | 422.6<br>(105.65)   |   |
| P - 36    | 14               | 22                      | 6.5                            | 20 ( 5)             | 23,800<br>( 5,950)   | 18.3         | 694<br>(173.4)      |   |
| P - 37    | 17               | 14                      | 5                              | 10 (2.5)            | 11,200<br>( 2,800)   | 22.4         | 62<br>( 15.5)       |   |
| P - 38    | 23               | 25                      | 10                             | 20 ( 5)             | 44,800<br>(11,200)   | 22.4         | 134.4<br>( 33.6)    |   |
| P - 39    | 25               | 25                      | 15                             | 80 (20)             | 500,000<br>(125,000) | 45.70        | 551<br>(137.75)     |   |
| P - 40    | 28               | 20                      | 13                             | 30 (7.5)            | 100,000<br>(25,000)  | 25.6         | 152<br>( 38)        | *****<br>Experiment stopped due to low culture potency  |
| P - 41    | June 1           | 10                      | 6                              | 50(12.5)            |                      | 8            | 222<br>( 55.5)      |   |
| P - 42    | 7                | 9.3                     | 8                              | 6 (1.5)             | 7,800<br>( 1,950)    | 16.3         | 31.3<br>( 7.825)    |   |



| Expt. No.   | Date of Refining | Culture charged (Liter) | Filtrated Culture for Refining |                     | Yield                |              | Potency* (Units/mg) | Remarks   |
|---|------------------|-------------------------|--------------------------------|---------------------|----------------------|--------------|---------------------|---|
|   |                  |                         | Volume (Liter)                 | Potency* (Units/cc) | (Units)*             | (Percentage) |                     |   |
| P - 43  | June 11          | 20                      | 11                             |                     | *****                | -            | -                   |   |
| P - 44  | 15               | 11                      | 8                              | 30 (7.5)            | 50,400<br>(12,600)   | 15.3         | 93.4<br>(23.35)     | *****<br>Vessel damaged<br>experiment<br>stopped. |
| P - 45  | 19               | 75                      | 50                             | 40 (10)             | *****                | -            | -                   |   |
| ( All products up to now were recrystallized on 22 Aug..) |                  |                         |                                |                     |                      |              |                     |   |
| P - 46  | 24               | 22                      | 20                             | 30 (7.5)            | 190,000<br>( 47,500) | 31.7         | 240<br>( 60)        |   |
| P - 47  | 27               | 23                      | 20                             | 50(12.5)            | 216,000<br>( 54,000) | 21.6         | 695<br>(173.75)     |   |
| P - 48  | July 1           | 62                      | 40                             | 50(12.5)            | 456,000<br>(114,000) | 22.8         | 579<br>(144.75)     |   |
| P - 49  | 3                | 60                      | 30                             | 50(12.5)            | 121,601<br>( 30,400) | 20           | 317<br>( 79.25)     |   |
| P - 50  | 7                | 70                      | 40                             | 40 (10)             | 236,225<br>( 59,056) | 24.5         | 535<br>(133.75)     |   |
| P - 51  | 10               | 26                      | -                              | -                   | -                    | -            | -                   | Due to contami-<br>nation.                        |
| P - 52  | 14               | 70                      | 40                             | 50(12.5)            | 520,000<br>(130,000) | 26           | 433<br>(108.25)     |   |
| P - 53  | 18               | 70                      | 50                             | 60 (15)             | 660,000<br>(165,000) | 22           | 670<br>(167.5)      |   |



| Expt. No. | Date of Refining | Culture charged (Liter) | Filtrated Culture for Refining |                     | Yield                |              | Potency* (Units/mg) | Remarks          |
|-----------|------------------|-------------------------|--------------------------------|---------------------|----------------------|--------------|---------------------|------------------|
|           |                  |                         | Volume (Liter)                 | Potency* (Units/cc) | (Units)*             | (Percentage) |                     |                  |
| P - 54    | July 21          | 80                      | 45                             | 50(12.5)            | 216,000<br>( 54,000) | 32.0         | 177<br>( 44.25)     |                  |
| P - 55    | 24               | 70                      | 40                             | 60 (15)             | 288,000<br>( 72,000) | 18           | 170<br>( 42.5)      |                  |
| P - 56    | 27               | 70                      | 50                             | -                   | 720,000<br>(180,000) | -            | 400<br>(100)        | Failure of assay |
| P - 57    | 30               | 70                      | 50                             | 60 (15)             | 490,000<br>(122,500) | 16.3         | 350<br>( 87.5)      |                  |
| P - 58    | Aug. 3           | 70                      | 40                             | 50(12.5)            | 359,000<br>( 89,750) | 18           | 468<br>(117)        |                  |
| P - 59    | 8                | 70                      | 45                             | 60 (15)             | 282,000<br>( 70,500) | 10.9         | 398<br>(99.5)       |                  |
| P - 60    | 12               | 70                      | 30                             | 60 (15)             | 253,000<br>( 63,250) | 14.0         | 910<br>(225)        |                  |
| P - 61    | 15               | 70                      | 46                             | (Assay failure)     | 153,000<br>( 38,250) |              | 308<br>( 77)        |                  |
| P - 62    | 19               | 70                      | 43                             | 60 (15)             | 77,200<br>(19,300)   | 13.6         | 372<br>( 93)        |                  |
| P - 63    | 22               | 70                      | 48                             | 50(12.5)            | 368,000<br>(92,000)  | 15.3         | 391<br>(97.75)      |                  |
| P - 64    | 25               | 70                      | 45                             | 40 (10)             | 400,000<br>(100,000) | 11.2         | 294<br>( 73.5)      |                  |



| Expt. No. | Date of Refining | Culture charged (Liter) | Filtrated Culture for Refining |                     | Yield                       |              | Potency* (Units/mg) | Remarks  |                                   |
|-----------|------------------|-------------------------|--------------------------------|---------------------|-----------------------------|--------------|---------------------|--|-----------------------------------|
|           |                  |                         | Volume (Liter)                 | Potency* (Units/cc) | (Units)* (Refining failure) | (Percentage) |                     |  |                                   |
| P - 65    | Aug. 28          | 70                      | 50                             | 60 (15)             | (Refining failure)          | -            | -                   | (**)<br>Experiment stopped due to low culture potency. |                                   |
| P - 66    | 29               | 75                      | 48                             | 50(12.5)            | 323,000<br>(80,750)         | 13.5         | 311<br>(77.75)      |  |                                   |
| P - 67    | Sep. 3           | 80                      | 50                             | 60 (15)             | 119,000<br>(29,750)         | 3.99         | 194<br>(48.5)       |  |                                   |
| P - 68    | 5                | 80                      | 60                             | 40 (10)             | 149,000<br>(37,250)         | 8.3          | 139<br>(34.75)      |  |                                   |
| P - 69    | 9                | 80                      | 50                             | 0                   | (**)                        | -            | -                   |  |                                   |
| P - 70    | 11               | 80                      | 50                             | 0                   | (**)                        | -            | -                   |  |                                   |
| P - 72    | 13               | 80                      | 35                             | 5 (1.25)            | 58,500<br>(14,625)          | 3.4          | 52.4<br>(13.1)      |  |                                   |
| P - 71    | 15               | 80                      | 40                             | 30 (7.5)            | -                           | -            | -                   |  | Trouble in freeze drying process. |
| P - 73    | 22               | 50                      | 30                             | 80 (20)             | 585,100<br>(146,275)        | 24.4         | 589<br>(147.25)     |  |                                   |
| P - 74    | 23               | 50                      | 27                             | 50(12.5)            | 52,900<br>(13,225)          | 3.9          | 126<br>(31.5)       |  |                                   |
| P - 75    | 25               | 50                      | 30                             | 50(12.5)            | 17,200<br>(4,300)           | 11.5         | 46.9<br>(11.725)    |  |                                   |
| P - 76    | 26               | 50                      | 25                             | 0                   | (**)                        | -            | -                   |  |                                   |
| P - 77    | 30               | 50                      | 20                             | 15                  | 44,300                      | 17.7         | 86.5                |  |                                   |



| Expt.<br>No. | Date<br>of<br>Refining | Culture<br>charged<br>(Liter) | Filtrated Culture<br>for Refining |                         | Yield    |              | Potency<br>(Units/<br>mg) | Remarks             |
|--------------|------------------------|-------------------------------|-----------------------------------|-------------------------|----------|--------------|---------------------------|---------------------|
|              |                        |                               | Volume<br>(Liter)                 | Potency *<br>(Units/cc) | (Units)* | (Percentage) |                           |                     |
| P - 78       | Oct. 1                 | 50                            | 23                                | 12.5                    | 7,960    | 2.9          | 17.1                      |                     |
| P - 79       | 2                      | 50                            | 20                                | 5                       | 4,820    | 4.82         | 12.0                      |                     |
| P - 80       | 3                      | 50                            | 25                                | 15                      | 19,500   | 4.32         | 16.0                      |                     |
| P - 81       | 3                      | 50                            | 25                                | 15                      |          |              |                           |                     |
| P - 82       | 5                      | 60                            | 35                                | 15                      | 136,700  | 24.9         | 148                       |                     |
| P - 83       | 6                      | 60                            | 35                                | 35.5                    | 237,000  | 19.1         | 126                       |                     |
| P - 84       | 7                      | 40                            | 25                                | 30                      | 41,700   | 5.54         | 89.3                      |                     |
| P - 85       | 8                      | 60                            | 35                                | 30                      | 189,500  | 18.1         | 152                       |                     |
| P - 86       | 9                      | 60                            | 37                                | 48.7                    | 0        | 0            | 0                         | Refining<br>failure |
| P - 87       | 10                     | 60                            | 37                                | 3.75                    | 42,000   | 30.2         | 34.3                      |                     |
| P - 88       | 13                     | 60                            | 31                                | 32                      | 202,000  | 20.4         | 194                       |                     |
| P - 89       | 19                     | 60                            | 39                                | 16                      | 243,000  | 38.9         | 193.7                     |                     |



| Expt. No. | Date of Refining | Culture charged (Liter) | Filtrated Culture for Refining |                     | Yield    |              | Potency* (Units/mg) | Remarks                 |
|-----------|------------------|-------------------------|--------------------------------|---------------------|----------|--------------|---------------------|-------------------------|
|           |                  |                         | Volume (Liter)                 | Potency* (Units/cc) | (Units)* | (Percentage) |                     |                         |
| P - 90    | Oct. 20          | 60                      | 44                             | 70                  | 920,000  | 29.5         | 520                 |                         |
| P - 91    | 21               | 60                      | 38                             | 51                  | 158,000  | 8.25         | 147                 |                         |
| P - 92    | 23               | 60                      | 30                             | 11.5                | 57,500   | 16.7         | 96                  |                         |
| P - 93    | 24               | 50                      | 18                             | 40                  | 415,000  | 5.76         | 152                 |                         |
| P - 94    | 25               | 60                      | 40                             | 70                  | 294,000  | 10.5         | 450                 |                         |
| P - 95    | 26               | 60                      | 40                             | 30                  | 157,000  | 13           | 157                 |                         |
| P - 96    | 27               | 60                      | 45                             | 32                  | 375,000  | 26           | 289                 |                         |
| P - 97    | 28               | 60                      | 48                             | 26                  | 653,000  | 522          | 340                 |                         |
| P - 98    | 29               | 60                      | 45                             | 26.7                | 378,000  | 31.5         | 166                 |                         |
| P - 99    | 30               | 100                     | 65                             | -                   | -        | -            | -                   | ) Not yet assayed       |
| P -100    | 31               | 100                     | 70                             | -                   | -        | -            | -                   |                         |
| P -101    | Nov. 1           | 100                     | 72                             | -                   | -        | -            | -                   |                         |
| P -102    |                  | 70                      |                                |                     |          |              |                     | } Culturing at present. |
| P -103    |                  | 70                      |                                |                     |          |              |                     |                         |
| P -104    |                  | 70                      |                                |                     |          |              |                     |                         |
| P -105    |                  | 70                      |                                |                     |          |              |                     |                         |



ANNEX 2

| Date charged | Volume of broth (liter) | Total powder penicillin (units) | No. of vials (per 30,000 units) | Volume broth per vial (liter) |
|--------------|-------------------------|---------------------------------|---------------------------------|-------------------------------|
| Oct. 1       | 2.3                     | 10,600                          | 0.3                             | 7                             |
| 2            | 20                      | 6,430                           | 0.2                             | 100                           |
| 5            | 35                      | 182,300                         | 6.1                             | 5.7                           |
| 6            | 35                      | 316,000                         | 10.5                            | 3.3                           |
| 7            | 25                      | 55,600                          | 1.9                             | 13.1                          |
| 8            | 35                      | 252,700                         | 8.4                             | 4.2                           |
| 10           | 37                      | 56,000                          | 1.5                             | <del>25</del>                 |
| 13           | 31                      | 269,000                         | 9                               | 3.5                           |
| 19           | 39                      | 324,000                         | 10.8                            | 3.6                           |
| 24           | 18                      | 55,330                          | 1.8                             | 10                            |
| 25           | 40                      | 392,000                         | 13.1                            | 3.1                           |
| 26           | 40                      | 209,330                         | 6.9                             | 5.8                           |
| 27           | 45                      | 500,000                         | 16.7                            | 2.7                           |
| 28           | 48                      | 870,670                         | 29.0                            | 1.7                           |
| 29           | 45                      | 504,000                         | 16.8                            | 2.7                           |



Process of ResearchinPenicillin Manufacturing Process

1, Nov. 1947

Nissin Chemical Co., Ltd.

In Feb. 1944, commenced investigation for fungi of good penicillin producing ability.

In March 1944, commenced research experiment on the penicillin process principally bacteriological research for a new micro-organism.

In March 1946, were shared three penicillin producing strains (No. 233, G1 and No. 176) and one assay test bacterium (Staphylococcus Aureus Terajima) from the Faculty of Agriculture, Tokyo University, and two assay test bacteria (Staphylococcus Aureus Terajima and St. A. Heatley) from the Faculty of Agriculture, Kyushu University, which enabled us to carry out comparison tests of the isolated strains and their penicillin producing abilities.

In June 1946, started research in the process of preparing penicillin in an industrial scale.

In Sept. 1946, the construction of the culture room and refining room completed.

In Oct. 1946, commenced research on the process of penicillin refining, and in order to supply penicillin broths



for it, work was started to produce 15 to 20 liter of culture per week as the goal.

In Dec. 1946, received two United States strains (B2 and Q176) through the generosity of Doctor Foster, Penicillin Consultant, Supply Division, SCAP.

In Jan. 1947, completed construction of the 100 liter per day capacity culture room for the surface (bottle) process.

In Feb. 1947, work commenced with the aim of executing experimental production of 10 liter per charge and 5 charges per week by the surface (bottle) culture process.

Apparatus for shaking culture installed.

In March 1947, applied to the GHQ, SCAP through the Ministry of Finance for approval to borrow funds (7,000,000 Yen) for the construction of the penicillin plant by tank process.

In April 1947, started enlargement of experimental production by the surface (bottle) method aiming at 20 liters per charge and 5 charges a week.

In July 1947, primary procedures for enlargement (to the goal of 70 liters per charge and 5 charges a week) of experimental production by the surface (bottle) culture method, commenced.

In Aug. 1947, the application submitted requesting permission to borrow funds was approved by AG 095 (28 July '47) ESS/AG (SCAPIN 4231-A). Work commenced on installing



facilities for preliminary test by the tank (submerged) method, i.e., 1 fermenter 250 liter size, and also preliminary work was commenced on the construction of the penicillin plant.

In Sept. 1947, submitted a part of experimentally produced penicillin to Sanitary Research Institute of the Ministry of Health for its potency assay test, although it qualified in the dissolving and Ph tests the figures for potency determined by our company by the dilution method was approximately three times larger than the potency assayed by the cylinder (cup) method in the central testing laboratory. (Potency units prior to those of Sept. 27th's given on annexed copies of laboratory data and receipt book were temporarily corrected as shown within parenthesis.)

In Oct. 1947, started enlargement of the experimental production with the aim to treat 50 liters of culture per day.

In Nov. 1947, the installation of the 250 liter fermenter for preliminary research work is scheduled to be completed by the middle of the month.



supply, <sup>Outlets</sup> Drugs Distribution Centers Under  
Temporary measures

Address

Manner

- (1) Tsukiyama cho  
Matsuyama City Joint Stock Co  
Matsuyama Shoten
- (2) 4 chome Minato Machi  
Matsuyama City Joint Stock Co  
Ogura Yakuban
- (3) Benten cho  
Matsuyama City Koichiro Wada
- (4) Nunomachi Doko  
Matsuyama City Sawaraba
- (5) Joban cho  
Imabari City Masashi Terao
- (6) 2 chome Motomachi  
Imabari City Ryoshu Kubo
- (7) Mamonouchi  
Uwajima City Tadachichi Ishizaki
- (8) Michi no machi  
Kata gun Yoshio Sano
- (9) Mishi horitata cho  
Matsuyama City Murakami Shoten

(over)



(10) Gunchu cho  
Dyo gun .

Maki ta Doi



臨時措置に依る荷事業者(卸賣業者)

住所 氏名

松山市築山町 株式会社 松中商店

" 港町四丁目 株式会社 小倉華館

" 辨天所 和田 幸一郎

" 道後湯之町 仙波 太郎

今治市瑞盤町 寺尾 正一

" 本所=丁目 久保 良 週

宇和島市丸の内 石崎 忠八

喜多郡内子町 佐野 義夫

松山市西堀端町 村上 商店

伊豫郡々中町 戸井 眞喜太



Subject; Distribution procedure of controlled medicines.

- (1.) - Notice is sent from the Central Medicines Control & Supply Co, to the Prefectural Medicines Control & Supply Co, as to the amount and sorts of medicines apportioned to the Prefecture. This notice of apportion is issued about 4 times a year; of course the notice indicates the supplies for each month.
- (2) Prefectural Medicines Control & Supply Co. inquires of the demanders (see notice 1) about the amount and sorts demanded.  
notice 1: Doctors' Association.  
Dentists' Association  
Veterinarians' Association  
Big Hospitals, Retail-dealers' union
- (3) Central Medicines Control & Supply Co, sends the medicines to the Prefectural Medicines Control & Supply Company.
- (4) Medicines received will be apportioned in accordance with the following procedures.

Conference is organized among the representatives of

the Prefecture, the hospital board and retail-dealers' union.



of course the notice indicates the supplies for each month.

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Dentists' Association  
Veterinarians' Association  
Big Hospitals, Retail-dealers' union

(3) Central Medicines Control & Supply Co. sends the medicines to the Prefectural Medicines Control & Supply Company.

(4) Medicines received will be apportioned in accordance with the following procedures.

Conference is organized among the representatives of doctors' associations, big hospitals and retail-dealers' union; in which the percentage apportioned to each of the three will be decided. After then, percentage to physicians, dentists and veterinarians will be decided in the same conference.

Prefectural Medicines Control & Supply Co. decides the percentage to each local retail-dealers' union without calling the conference.

Prefectural doctors' association decides the percentage to each local chapter, and each chapter decides the amount  
(To Be Continued)



and sorts to private doctors.

(5) Chapter of Prefectural Doctors' Association, <sup>and</sup> Medicines Retail-dealers' union submit the report on the final decision of medical supply to the Prefectural Medicines Control & Supply Co., and notify it to each demander.

(6) Prefectural Medicines Control & Supply Co. distributes the medicines directly to the demanders in accordance as the percentage decided after the above-mentioned procedures.



Supply Co., and notify it to each demander

- (b) Prefectural Medicines Control & Supply Co. distributes the medicines directly to the demanders in accordance with the percentage decided after the above-mentioned procedures.



~~Supply~~

Jap. Army and Navy Supplies -  
Lost supplies sold Nov '46  
¥ 300,000 value.

None left. (?)

These drugs were distr. to private  
doctors and hosp. through  
Distribution Company.

There are 2 national Hosp in Kan.  
One General and one TBC.

In March 1946 stocks of Nat'l  
Hosp. were inventoried - No  
excess stock was discovered.

Curator Produced + Controller  
Medicine -

Man in charge Distr. (Fujita)  
should prepare allocation  
of drugs. This is done monthly.  
Says he spot checks  
private doctors to see if  
distr. is satisfactory.



You value of Controller med.  
 disto in 1946 is 12 Million -  
 Value of med in whole  
 now is 2.5 million -

Procedure for Doctor to  
 Purchase Emergency Med.

- ① Request Supply Co (Cities)
- ② " " Health Center (rural)

Each doctor should be notified  
 by letter, telling them procedure  
 to use in procuring emergency  
 drugs -

How do doctor pay for Medicines?  
 Either cash or frozen checks -

There are 124 Controller Medicines -  
 How doctor have to part  
 in request, or does he get  
 supplies automatically - ?



Doctor requests —

2 Jap. produced penicillin  
rec'd in this prefecture —

30 ampules (30,000 in each)  
have been rec'd.

This distr. to hosp. will  
be a number of over 200.

This supply has not been  
distr. — kept in Ken office.

This prefect. will receive

14130 Can. foot powder — <sup>0.06</sup>

42 5 gal drums. ethyl alcohol

~~46~~ 32500 Tablet Sulfathiazole (Jap.)

have been rec'd.

23,000 for V.D.

9,500 other diseases

} rec'd 22 Nov.

From now on (after initial  
supply) will be requisitioned  
on a monthly basis —



Rosenhan

Neopharm - 1000 Amps  
 Besmuth - 0  
 Sulfathiazole - 0

Population 18% of  
 Use this as a basis for  
 ordering drugs for diseases  
 other than V.D.

If no satisfaction about  
 vaccines - then is plenty  
 of vaccine available -

Agricultural Hospital (Nuygawa)  
 (check to see if  
 supplies come from -  
 O Agricultural Com.  
 O Kew -

What % of controller med. are  
 allocated to retail drug stores -  
 20% approx.



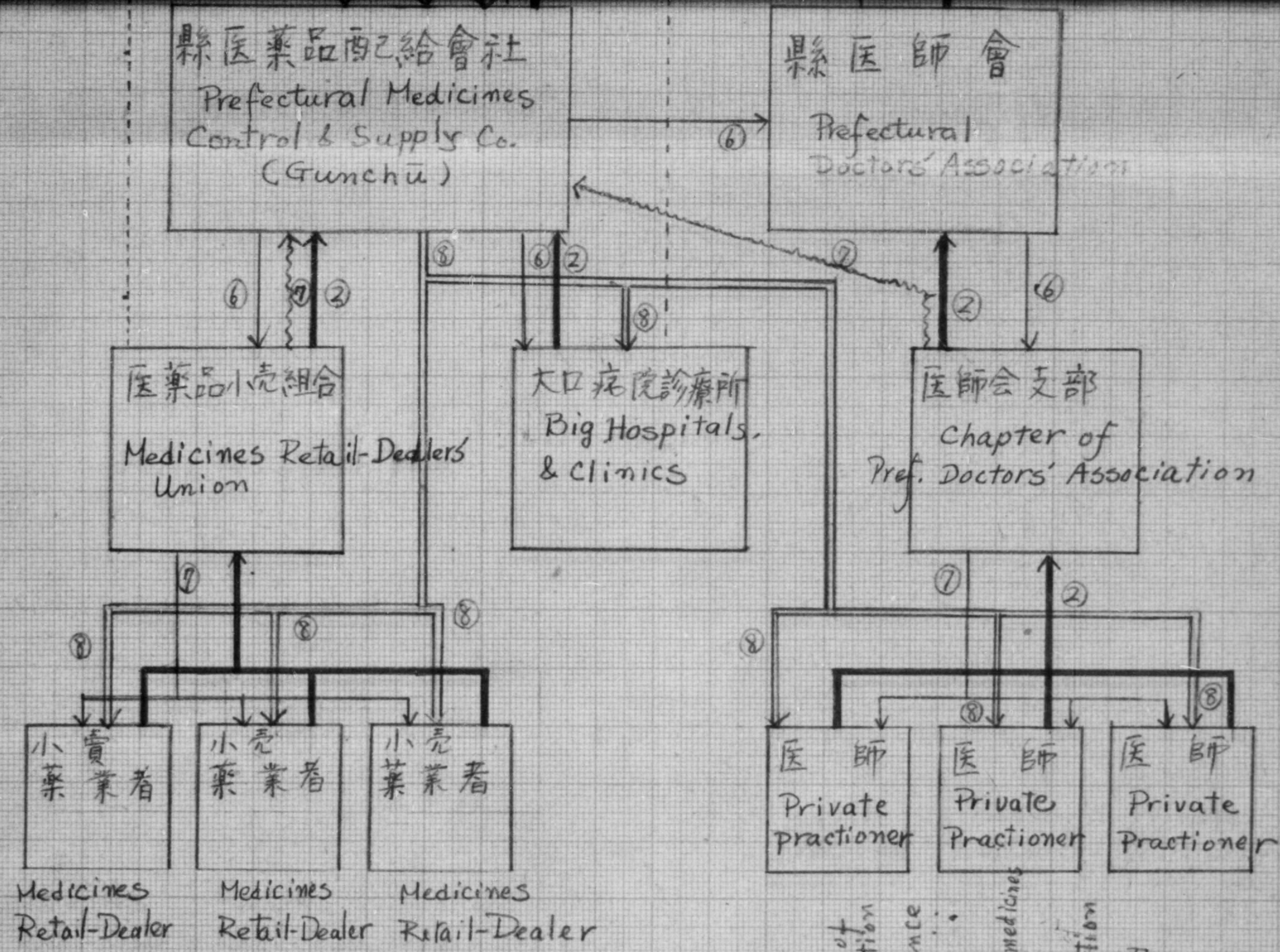
Laboratory studies -  
first submit request  
to Commerce & industry -  
if no luck try Welfare  
Ministry. Action also -

Allocation









Notification of apportionment  
 割当通知  
 Conference  
 協議  
 Supply of medicines  
 現品  
 Report of apportionment  
 割当報告  
 Demand  
 要求



*Supply, prefectures*

1947 Distribution Plan of Pyrethrum Emulsion (30X)

| Name of Prefecture      | Allocation for Populace<br>in Cities |                                   | Allocation for Occupa-<br>tion Area               |                     | Total of<br>Alloca-<br>tion<br>Pref. |
|-------------------------|--------------------------------------|-----------------------------------|---|---------------------|--------------------------------------|
|                         | Permillage<br>of City<br>Populace    | No. of Drum<br>Cans<br>(50 gals.) | Permillage of<br>Allied Stationed<br>Major Cities | No. of Drum<br>Cans |                                      |
| Hokkaido                | 44.7                                 | 532                               | 43.0  | 73                  | 605                                  |
| Aomori                  | 9.4                                  | 112                               | 9.0   | 15                  | 127                                  |
| Iwato                   | 7.3                                  | 87                                |   |                     | 87                                   |
| Miyagi                  | 14.8                                 | 176                               | 27.0  | 46                  | 222                                  |
| Akita                   | 6.7                                  | 80                                |   |                     | 80                                   |
| Yamagata                | 10.5                                 | 125                               |   |                     | 125                                  |
| Fukushima               | 8.7                                  | 103                               | 6.0   | 10                  | 113                                  |
| Ibaragi                 | 6.5                                  | 77                                |   |                     | 77                                   |
| Tochigi                 | 10.5                                 | 125                               |   |                     | 125                                  |
| Gunma                   | 13.7                                 | 163                               |   |                     | 163                                  |
| Saitama                 | 17.7                                 | 211                               |   |                     | 211                                  |
| Chiba                   | 20.0                                 | 238                               |   |                     | 238                                  |
| Tokyo                   | 159.9                                | 1853                              | 356.0   | 605                 | 2458                                 |
| Kanagawa                | 62.5                                 | 744                               | 73.0  | 124                 | 868                                  |
| Niigata                 | 15.3                                 | 182                               | 15.0  | 25                  | 207                                  |
| Toyama                  | 10.7                                 | 127                               |   |                     | 127                                  |
| Ishikawa                | 13.7                                 | 163                               |   |                     | 163                                  |
| Fukui                   | 3.4                                  | 40                                |   |                     | 40                                   |
| Yamanashi               | 3.9                                  | 46                                |   |                     | 46                                   |
| Nagano                  | 14.1                                 | 168                               | 9.0   | 15                  | 183                                  |
| Gifu                    | 12.4                                 | 147                               | 15.0  | 26                  | 173                                  |
| Shizuoka <i>NICHOLS</i> | 24.8                                 | 295                               |   |                     | 295                                  |
| Aichi                   | 52.5                                 | 625                               | 74.0  | 126                 | 751                                  |
| Mie                     | 17.7                                 | 211                               |   |                     | 211                                  |
| Shiga                   | 7.2                                  | 86                                |   |                     | 86                                   |
| Kyoto                   | 46.6                                 | 554                               | 94.0  | 150                 | 714                                  |
| Osaka                   | 87.4                                 | 1040                              | 134.0   | 226                 | 1266                                 |
| Hyogo                   | 48.5                                 | 577                               | 46.0  | 76                  | 653                                  |
| Nara                    | 3.1                                  | 37                                |   |                     | 37                                   |
| Wakayama <i>GATES</i>   | 11.3                                 | 134                               |   |                     | 134                                  |
| Tottori                 | 4.6                                  | 55                                |   |                     | 55                                   |
| Shimane                 | 6.1                                  | 73                                |   |                     | 73                                   |
| Okayama                 | 10.7                                 | 127                               | 11.0  | 19                  | 146                                  |
| Hiroshima               | 22.4                                 | 267                               | 18.0  | 31                  | 298                                  |
| Yamaguchi <i>CRITCH</i> | 30.9                                 | 363                               |   |                     | 363                                  |
| Tokushima               | 3.9                                  | 46                                | 9.0   | 15                  | 61                                   |
| Kagawa                  | 6.7                                  | 80                                |   |                     | 80                                   |
| Ehime                   | 15.3                                 | 182                               |   |                     | 182                                  |
| Kochi                   | 5.6                                  | 67                                |   |                     | 67                                   |
| Fukuoka                 | 54.7                                 | 651                               | 30.0  | 51                  | 702                                  |
| Saga                    | 4.7                                  | 56                                |   |                     | 56                                   |
| Nagasaki <i>CRITCH</i>  | 21.9                                 | 261                               | 18.0  | 31                  | 292                                  |
| Kumamoto                | 15.0                                 | 178                               |   |                     | 178                                  |
| Oita                    | 12.8                                 | 152                               |   |                     | 152                                  |
| Miyazaki                | 9.3                                  | 111                               |   |                     | 111                                  |
| Kagoshima               | 9.9                                  | 118                               | 13.0  | 22                  | 140                                  |
| <b>Total</b>            | <b>1000.0</b>                        | <b>11900</b>                      | <b>1000.0</b>                                     | <b>1700</b>         | <b>13600</b>                         |



SUPPLY PROCEDURES AND PROBLEMS

At the time of the occupation, the Japanese Government did not have a national level plan for the supply of materials required in carrying out disease control programs. Local officials were responsible for securing such items as they considered necessary. As a result, there was no uniformity among the various prefectures, most of the materials used were of questionable value and no appreciable amount of supplies and equipment were ever made available.

With the development of a large scale Insect and Rodent Control Program, early in 1946, the need for a comprehensive supply plan was recognized. In accordance with the general policy of utilizing indigenous facilities and supplies to the fullest extent, it was decided that emphasis would be placed on the use of pyrethrum base insecticides insofar as possible. Japan has been a source of world supply for pyrethrum for a number of years and considerable stocks of pyrethrum flowers could be made available. It was necessary, also, to initiate production of spraying and dusting equipment. While this equipment had been produced in quite large quantity for agricultural purposes, no particular attention had been given to manufacture or allocation for disease prevention programs.

Although the 1946 program started late, the results were fairly good and substantial quantities of pyrethrum emulsion, phenothiazine, other miscellaneous insecticides and the necessary equipment were produced and distributed. It was necessary to use some U.S. produced equipment. This equipment was distributed through occupation forces supply channels and released to Japanese health authorities at the prefectural level.

Insofar as the 1947 program is concerned, the Japanese Ministry of Health and Welfare has been organized to produce and distribute all necessary supplies and equipment. It will not be necessary to distribute any items through occupation forces supply channels and instructions to that effect have been issued to the Commanding General, Eighth Army.

Under the general supply plan, the Ministry of Health and Welfare (Pharmaceutical Affairs Section) is responsible for production and distribution to prefectures. In the development of a production plan, the Welfare Ministry estimates national requirements and submits to Public Health and Welfare Section for review. When decision has been made as to production quotas, a bill of materials is prepared. Items which cannot be made available locally are scheduled on the import program. It is necessary to import all petroleum products. In the past the same situation has applied in the case of DDT. However, local production of DDT concentrate has been initiated and present production is averaging approximately 10 tons monthly (about 20% of requirements). Production capacity is sufficient to meet the needs of the nation and future production is dependent entirely upon availability of raw materials. Facilities have been developed for the manufacture of DDT dust and spray and no



further imports of finished materials are contemplated. With the exception of DDT, all other materials are being completely manufactured in Japan. Actual distribution procedures vary somewhat for the different items, but generally speaking, the Welfare Ministry either moves the supplies to prefectures under a national distribution plan or notifies the prefectures as to the source in which the materials may be obtained and the amount authorized for purchase. Prefecture officials are responsible for receipt, storage and issue of all items. The Welfare Ministry has notified all prefectures of the materials available and the procedure which should be followed in obtaining the required supplies and equipment.

Financing of all disease control programs has presented a number of problems. As previously mentioned, these programs have never before been attempted on a national scale, and it may be expected that prefectures will be concerned over cost of the programs and procedures to be followed in securing necessary funds. Public Health & Welfare Section has insisted that financing be arranged in such a manner that there will be no interruptions in production and distribution of necessary materials. The question as to financial responsibility between the national government and the prefectures is one to be determined by the Japanese Government. Since questions on financial procedures will arise from time to time, it is desirable that Military Government officers have a general idea of the procedural plan. The central government has provided an appropriation for the importation, production and distribution of DDT products. This simplifies to a considerable extent the supply problem since prefectures may secure DDT without advance payment. The Ministry of Welfare intends to assess prefectures 50% of the cost of DDT products. I would like to emphasize, however, that this is an assessment which will be paid to the Japanese Government at some later date. We have been informed that no prefectures have as yet reimbursed the central government for DDT purchases. With the exception of DDT the central government has not as yet appropriated funds to cover the insect and rodent control program. It is necessary therefore that prefectures purchase such items as pyrethrum emulsion, rat poison, phenothiazine, other miscellaneous insecticides and spraying and dusting equipment on a commercial basis from dealers designated by the Japanese Government. Generally speaking the Welfare Ministry produces and directs shipment to prefectures who are responsible for payment upon receipt. In this connection I would like to add that it is extremely important that prefectures appropriate the necessary funds and settle their accounts promptly since manufacturers and distributors are receiving no financial assistance from the Government.

The following is a list of materials that are available for Insect and Rodent Control programs:

|  |                |
|--|----------------|
| 10% DDT dust   | 5,000,000 lbs. |
| 5% DDT spray   | 400,000 gals.  |
| (Additional 500,000 gals. to be mixed with fuel oil now in planning stage - Production can be accomplished very rapidly provided petroleum products and containers can be made available.) |                |
| DDT dusters  | 100,000 each   |
| Sprayer, knapsack, 3 gal.  | 50,000 "       |



|  |              |
|--|--------------|
| Sprayer, pump type, semi-automatic   | 20,000 each  |
| Sprayer, hand type, $\frac{1}{2}$ gal.   | 50,000 "     |
| Pyrethrum emulsion - approximately 750,000 gallons scheduled for production or 22,000,000 gals. of spray when diluted with 30 parts water. |              |
| Rat poisons (antu and nekeirazu)   | 125 tons     |
| Rat traps (spring type and cage type)  | 500,000 each |

(Several thousand U.S. produced knapsack and hand type sprayers, a residue of the 1946 program, will be available. This equipment has been released to the Japanese on an import basis and will be distributed concurrently with Japanese produced items).

It will be noted that both pyrethrum emulsion and DDT products are available. As previously mentioned the great majority of DDT dust and spray used in Japan is being manufactured from concentrate imported from the United States. For this reason pyrethrum products should be utilized whenever insecticides of this type will provide a satisfactory end result. DDT is available in sufficient quantities for those uses in which DDT products are particularly indicated.

DDT products are distributed through a series of regional warehouses located in strategic areas throughout Japan. The Ministry of Welfare directs the shipment of DDT to these warehouses and maintains the necessary stock level. Prefectural health authorities are responsible for scheduling requirements of DDT and ordering the specific quantities required by direct application to the Ministry. The Ministry notifies prefectures as to amounts approved for sale and at the same time directs the appropriate regional warehouse to make shipment. Local government officials advise the Ministry of the point at which shipment should be made and assumes responsibility upon arrival of material at the shipping point. In this connection, it might be mentioned that the supply of containers is one of the most critical items in this program and the Welfare Ministry has directed prefectural authorities to return all empty containers to the manufacturers whose name is stamped thereon. Expenses for return of empty containers are borne by the manufacturers.

A detailed chart covering the importation, manufacture and distribution of DDT is attached as a matter of information.

The Welfare Ministry has designated a central agency, composed of manufacturers, to handle distribution of pyrethrum emulsion, based on a nation-wide distribution program. Allocations have been made to the various prefectures and manufacturers have been instructed to ship without request from prefectures. As in the case of DDT, local health authorities are responsible for receipt, storage and issue within the prefecture. A chart showing the detailed distribution procedure is attached.

Spraying equipment is distributed in a manner similar to that outlined for pyrethrum emulsion. The Ministry prepares a production plan, allocates specific amounts to prefectures and directs manufacturers to ship without request from local authorities.



The Welfare Ministry has designated a central commercial agency as the organization responsible for distribution of rat poison. This company maintains branches in all prefectures and the Ministry prepares an allocation plan covering amounts to be furnished individual prefectures. Based on this plan prefectures are responsible for purchase of rat poison from local distributing companies under normal commercial practice. A chart outlining distribution channels is attached.

I have outlined in a general manner the system that has been developed for supply of the Insect and Rodent Control program. Experience gained during 1946 indicates that the plan is workable and that the Japanese Government is capable of producing and distributing necessary supplies and equipment. It must be remembered, however, that it is a new departure in Japan and that constant supervision and guidance is necessary by Military Government personnel both at the national and prefectural levels. The Supply Division, Public Health & Welfare Section, exercises guidance and supervision to insure that materials are made available to prefectures. In carrying out this responsibility it has been found that the development of a comprehensive plan is a first step. Once the plan is completed, it is then necessary to constantly check actual production and distribution. As has been outlined above, operating responsibility of the Ministry of Welfare ceases at the prefectural level and it is extremely important that prefectural health authorities develop a plan and organization to cover distribution activities. The Welfare Ministry has notified prefectures of the overall operating plan, also the specific quantities of materials that are available. Any question which may arise in this connection may be settled by prompt communication with the Pharmaceutical Affairs Section, Ministry of Health & Welfare. It is recommended that each prefecture be required to implement the supply plan of the Welfare Ministry immediately and to outline detailed operating procedures covering the ordering, receipt, storage and issue of materials necessary for the Insect and Rodent Control program. Provision of adequate funds is another matter that must be settled promptly. From your past experience, I am sure you will realize that constant supervision and guidance will be necessary by Military Government officials to insure satisfactory accomplishment of the program. Public Health & Welfare Section will continue to keep you informed of latest developments through the medium of the Weekly Bulletin. Any problems which cannot be solved locally or by communication with the Welfare Ministry should be made the subject of a special report through military government channels.

I would like to take this opportunity of discussing briefly narcotic control and some of the other phases of supply in which Public Health & Welfare Section is engaged.

I am sure that you are familiar with the overall narcotic control program and the excellent progress that has been made. Narcotic control in Japan is proving to be such an effective measure that loss of narcotics by theft and burglary to illicit channels for addiction purposes is assuming more and more importance. Constant vigilance to prevent such loss is of the utmost importance, since by their very nature narcotics are extremely difficult to recover. Hospitals which have reported large



narcotic losses by burglary recently have been required to provide safes for proper storage before being permitted to order new stock. In several cases hospitals have provided the safes on their own initiative immediately after experiencing such a loss. Effort should be made to have all hospitals carrying a sizable narcotic stock to provide safes for storage before the burglary occurs.

Another method to curtail such loss of narcotic is to insist to procurators that 10 to 12 months imprisonment be demanded for all addicts apprehended for violation of the narcotic laws. This will prove effective in curing the addict of his addiction as well as removing a potential source of thievery, burglary and other crimes.

Registered local wholesalers throughout Japan may purchase necessary narcotics from registered Central Wholesalers in Tokyo and Osaka. Local wholesalers should hold stocks to not more than a six months' supply level and must provide safe storage. Stocks are on hand for all the legitimate medical needs of the Japanese people but diversions for any other use must be stopped.

The present economic situation in Japan directly effects the production of medical supplies and equipment, as well as other commodity groups. Pharmaceutical production capacity in Japan is adequate to cover normal domestic needs but the shortage of raw materials, fuel and power has served to make it very difficult to maintain a satisfactory production level. At the present time the Japanese Government, under the supervision and guidance of SCAP, is setting up and placing in operation a new system of production control. Briefly, the program provides for the elimination of the numerous control associations that have exercised authority in the past over the allocation of raw materials to industry with government sanction. An Economic Stabilization Board has been created with a ministry status. This board will assume complete authority for developing an overall production program and allocating critical raw materials for its accomplishment. Direct supervision over production will remain with the various ministries and in the case of medical and sanitary supplies, the Welfare Ministry will be charged with allocating the raw materials, provided by ESB, to individual manufacturers. Under this system it will be possible to exercise better control over the allocation of critical raw materials and regulate the production of essential supplies and equipment.

The production of vaccines has reached a fairly satisfactory level. The only remaining item which is being imported is typhus vaccine and from present indications, it will be possible to eliminate this item from the import list in the very near future. As you know, a very large typhoid vaccine production program is now in process and close supervision and guidance on the part of all concerned will be necessary to produce the substantial amount of vaccine that will be required for the mass immunization program.

The production of sulfa drugs is increasing. The largest production is still confined to sulfanilamide. During March approximately 2½ tons of sulfathiazole was manufactured. Production has been hampered somewhat



by patent restrictions and shortage of fuel. At present only one firm in Japan is licensed to produce sulfathiazole under foreign patents. The company controlling the patent will not license additional factories. Several other plants are producing under Japanese patents and officials of the Welfare Ministry are of the opinion that the quality is equal to that of foreign manufacture. The Japanese do not know the technique of sulfadiazine manufacture and we have been unable to secure a release of patent rights from the U.S. In the meantime small quantities are included on the import program.

Mapharsen and bismuth subsalicylate are now in production and it is expected that adequate amounts will be available for distribution in the near future. Standardization of these drugs is the greatest problem at present.

There is an adequate supply of x-ray film available which may be purchased through normal commercial channels. The Welfare Ministry has disseminated information concerning sources of supply. Any prefecture that is experiencing difficulty in x-ray film supply should immediately communicate with the ministry. Chemicals for development also are available. In addition to normal Japanese needs of x-ray film, production quotas have been set-up for supply of a portion of occupation forces requirements in Japan, Korea and the Ryukyus. An export program has been established for minimum civilian requirements in Korea. Sufficient 35 mm film is in production to cover requirements of the anti-tuberculosis campaign now in process in Japan. The necessary photographic machines also are in production and schedules are being met.

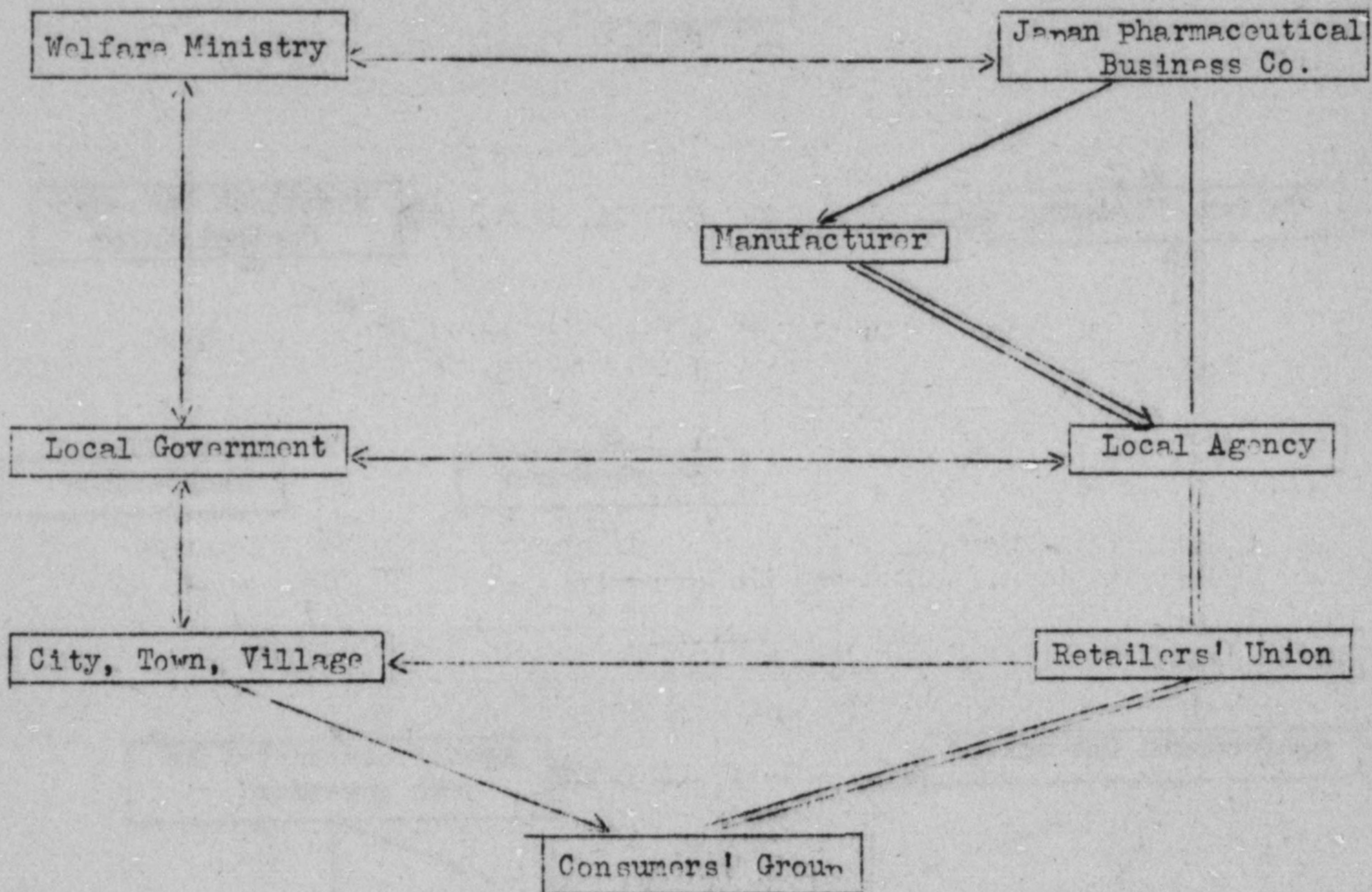
The Japanese Government has allocated ten million pounds of imported cotton for the purpose of manufacturing absorbent cotton and surgical dressings for the year ending 30 September 1947. Twenty million pounds will be allocated for each of the following two years. Absorbent cotton is now in process of distribution under this program. The production of gauze and bandages has been slow but it is expected that increasing quantities will become available during the next 60 days.

Production of penicillin during March totalled 265,000,000 units. This is of course only a fraction of minimum requirements. A number of manufacturers have completed preliminary plans for deep tank production and one pilot plant is in operation with several others under construction. Large scale production cannot be expected until the industry is set up for deep tank manufacture. This is a highly technical operation and much remains to be accomplished before volume production is attained.

The entire Japanese distribution control system is being revamped and set up under the Economic Stabilization Board. Control associations are being eliminated and their functions will be assumed by the responsible ministry under supervision and regulations of the ESB. Medical supplies and equipment, in short supply, will be distributed on a ration basis, which it is expected will eliminate most of the difficulties and delays experienced under the present system. It will take several months to install the ration system and in the meantime every effort must be made to force distribution of available supplies to using agencies under the present distribution system.



DISTRIBUTION CHANNEL OF ANTUF DRUG

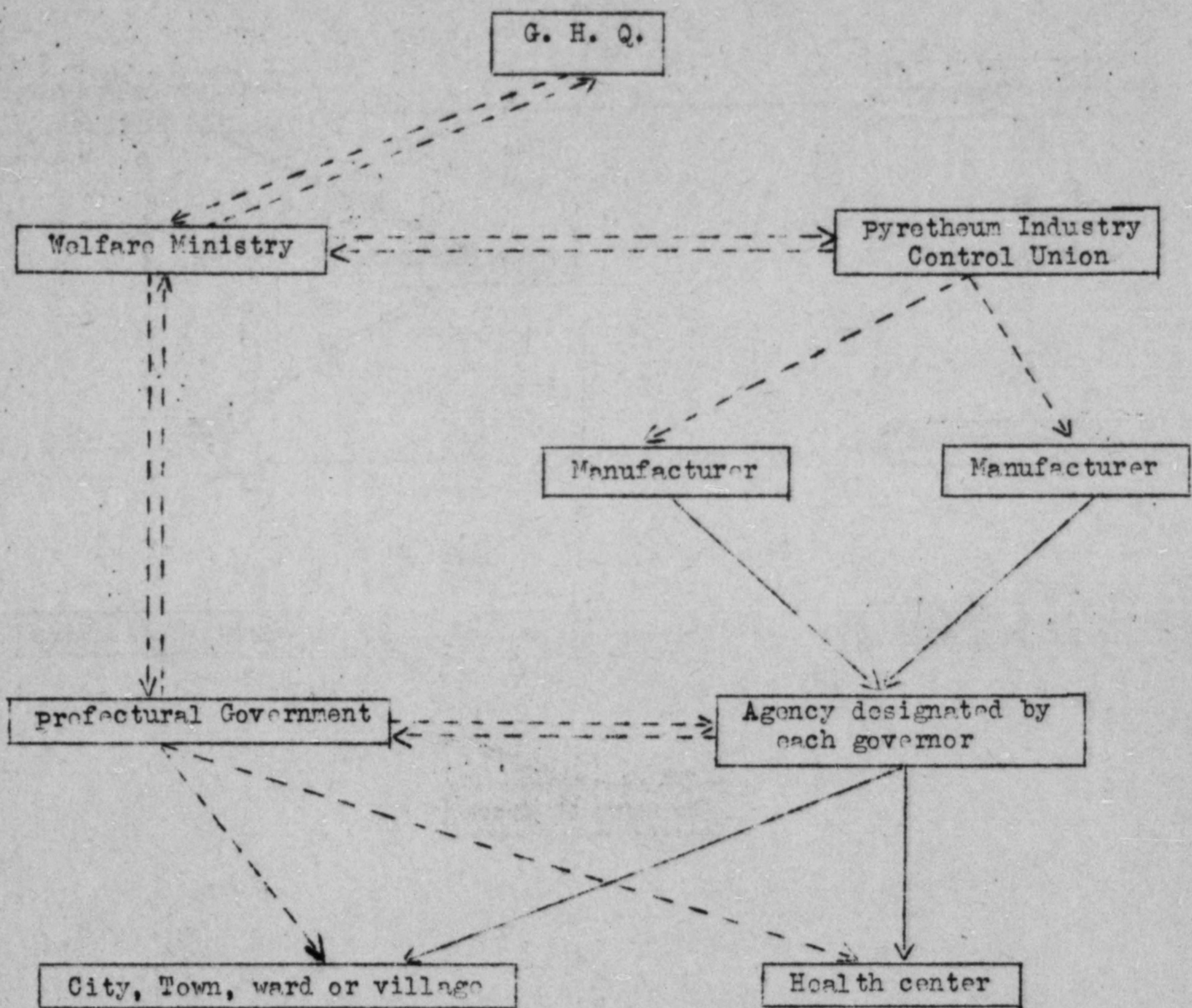


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DISTRIBUTION CHANNEL OF PYRETHEUM EMULSION

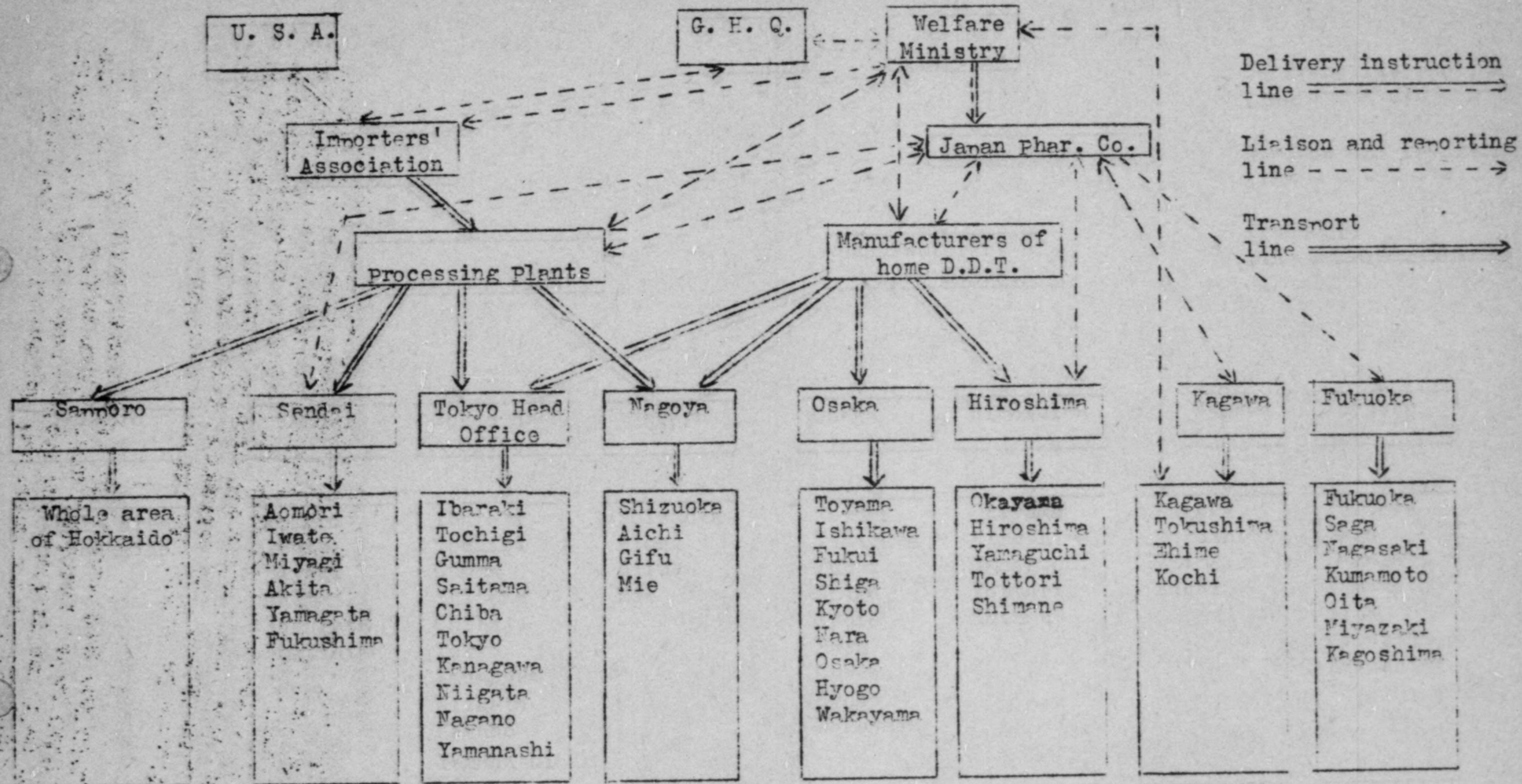


-----> Liaison and report line

—————> Transport line



DISTRIBUTION CHANNEL OF D.D.T.





The Japanese Government has assumed complete responsibility for the distribution of imported medical and sanitary supplies and equipment. This completes action on the plan initiated during October 1946 to relieve occupation forces units of further responsibility for civilian supply.

This brief outline covers the highlights of narcotic control and medical and sanitary supply production and distribution in Japan at the present time. Progress in narcotic control has been outstanding. Substantial progress also has been made from the supply standpoint. The supervision and guidance exercised by military government officers in the field has contributed materially to the success of these programs and will be necessary in effecting further improvement.



LIAISON SECTION  
EHIME KEN

public health/wakase

12 Mar., 1948

TO : Capt. Lawrence, Ehime Mil Govt Team  
FROM : Chief of Public Health sect., Ehime Ken  
SUBJECT: Plan how to control aquatic foodstuffs.

I beg to submit to you the subject plan as attached  
for your information.

K. Tsuzuki  
Chief of Public Health sect.,  
Ehime Ken

1 Incl: plan how to control  
aquatic foodstuffs

F:I



Plan How to Control Aquatic Foodstuffs

I. The plan aims at the sanitation of processed aquatic products in compliance with the Food Hygiene Law and the request of SCAP.

II. The aquatic foodstuffs mean all the aquatic animals which are produced in salt or fresh water and are served as food.

The processed aquatic products mean fresh, salted, frozen, smoked, dried, kneaded or canned animals described above.

The aquatic foodstuffs market means all the facilities where aquatic foodstuffs are sold.

The aquatic foodstuffs stores, processing plants and canning or bottling plants mean all the selling, handling, preserving and processing places of aquatic foodstuffs.

The dealers mean the persons whose business is to sell, handle and process the aquatic foodstuffs.

The inspector means a food hygiene inspector appointed by the governor.

III. The dealers are requested to comply with the instructions of inspectors for the sanitation of the aquatic foodstuffs.

IV. The method of inspection designated in Chapter 5 of the Food Hygiene Law shall be as follows.

1. <sup>Aquatic</sup> ~~Marine~~ foodstuffs and their market;

a) The inspector will try to discover the foodstuffs of lower freshness and rotten ones;

b) The inspector will try to maintain the freshness of the foodstuffs.

1) He will not allow anyone to divide the load anywhere outside the designated place.

2) He will not allow anyone to tread his feet upon the load.

3) Fish shall not be disposed of on the earth.

4) The foodstuffs shall not be left for a long time under the hot sunshine.

5) Disposal and division of the load shall be performed quickly.

6) The foodstuffs shall not be loaded on trucks in bulk.



- 7) A suitable quantity of ice shall be used.
- c) The inspector will try to maintain cleanliness.
  - 1) Sweeping and cleanliness shall be maintained inside the market.
  - 2) Receptacles and balances shall be kept clean.
  - 3) Urination and spitting inside the market shall be refrained from.
  - 4) The instrails and bone of fish or shells shall not be thrown away carelessly.
  - 5) Swellfish shall not be allowed to be taken out of the market unless after their entrails were removed at the designated place.
  - 6) The ditch shall always be swept cleanly.
  - 7) Fly prevention facilities shall be installed.
  - 8) Potable water shall be prepared abundantly.

2. Aquatic foodstuffs stores;

- a) Fly prevention facilities (such as cover) shall be prepared.
- b) Freshness shall be maintained.
  - 1) Ice-box shall be installed and the foodstuffs shall not be preserved anywhere except there.
  - 2) The place where entrails are removed shall be kept clean so that rotten smell will be reduced.
- c) Cleanliness shall be maintained.
  - 1) Cleanliness will be the first thing inside the store.
  - 2) Receptacles and balances shall be kept clean.
  - 3) Clean aprons shall be used.
  - 4) The floor shall always be washed by free use of potable water.



### 3. Aquatic foodstuffs processing plants:

- a) Fly prevention facilities (such as cover) shall be prepared.
- b) The material shall be handled cleanly and its sanitary condition shall be checked.
- c) Receptacles of the material shall not be put on the earth.
- d) Cooking table on which fish paste is manufactured shall be kept clean.
- e) The inspector will take away some of the cereals, starch or other additionals at his option to check on its purity.
- f) Receptacles for finished foodstuffs shall be clean and dry.
- g) Clean caps and aprons shall be used by all the employees.
- h) Something impermeable shall be used as the floor of the plant.
- i) Nobody except employees shall enter the plant while at work.
- j) No animal shall be allowed to enter into the plant.
- k) The employees shall wash their hands before setting to work.
- l) Clean toilet shall be installed and a notice requesting the employees to wash their hands after stool shall be pinned up there.

### 4. Aquatic foodstuffs canning and bottling plants:

- a) Receptacles of materials shall be kept clean.
- b) The material shall be well washed.
- c) All the water used should be potable.
- d) The receptacles for waste materials should not be leaky.
- e) The material should be kept thoroughly cool in the ice box.



- e) All the receptacles used during process should be kept clean.
- g) All the cans and bottles should be thoroughly sterilized in steam prior to use.
- h) If anything wrong is found with the can or bottle, it should be removed out of the line.
- i) The temperature of steam should be kept correct.
  - 1) A correct thermometer should be installed.
  - 2) It should be inspected if the time and temperature are fit for sterilization.
  - 3) The manager of the plant is requested to submit a report to the inspector on the time and temperature for sterilization.
- j) Clean caps and aprons should be used by employees.
- k) The use of dirty finger-cap or bandage by employees should be prohibited.
  - 1) Fly prevention facilities should be used.
  - m) The floor should be made of impermeable material and be kept clean all the time by washing it with water.
  - n) The employees should wash their hands before setting to work.
  - o) Walls and ceilings should be kept clean.
  - p) Suitable method of lighting and ventilation should be adopted.
  - q) Clean toilet should be installed and a notice requesting the employees to wash their hands after stool should be pinned up.
  - r) The inspector will check if the sample for export squares with the manufacturing specification.
  - s) The inspector will examine condiments and oil used in processed food.

##### 5. Freezing plant:

- a) Receptacles for aquatic foodstuffs should be limited to those which never contained poisonous goods.



b) Foodstuffs should not be frozen together with other materials.

c) The passage and floor should be kept clean and soiled foodstuffs should be treated as dirt.

V. When something harmful to the public health is found about aquatic foodstuff, processed one, market, store or processing, canning or bottling factory, the inspector is required to take the following action:

1. Concerning aquatic foodstuffs which do not come up to the standard in freshness.

a) When they are fresh enough to be processed, although they are not good enough to be distributed among homes in general, he must order them to be used as processing material after consultation with the Ken fisheries inspector.

b) When they are not fit to be processed, he must order them to be used as feed for live-stock or fertilizer after consultation with the Ken fisheries inspector.

c) When a trader finds them not to come up to the standard in freshness, the trader must be directed to report on their species, quantity destination, disposal etc.

d) When a store, processing factory or other installation is found to be against the regulations, the owner or responsible person must be admonished of it on the spot.

e) When the above installation is found several times to be against the regulations regardless of admonition, he must take action in accordance with the law.

2. Concerning inferior aquatic foodstuffs and processed aquatic foodstuffs.

a) When aquatic foodstuff or processed one is found to be of poor quality, a necessary quantity of it must be taken away for examination.

b) An amount to be taken away for examination cannot exceed what is necessary for the purpose.

c) In case of taking it away for examination, a certificate in the attached form No. 1 must be delivered to attest the fact.

d) The results of the examination must be reported to the prefectural governor in the attached form No. 2.



e) Aquatic foodstuff or processed aquatic foodstuff found harmful to health must be abandoned as well as prohibited from being sold.

f) In case the above foodstuff is ordered abandoned, it must be reported to the prefectural governor in the attached form No. 3 stating reason for the order of abandonment and a copy of the report must be delivered to the receiver of the order of abandonment.

g) One who sells the raw or processed aquatic foodstuff prohibited from sale or ordered abandoned must be dealt with according to the law.

3. Concerning unsanitary facilities:

a) Defective points must be specified and ordered to be improved.

b) Necessary time for the improvement must be given, and inspection must be made again after the expiration.

c) In case the order of improving facilities harmful to the public health is neglected, a step must be taken to prohibit their use.

d) One who uses the facilities prohibited from using must be dealt with according to the law.



(Attached paper)

Form No. 1

Certificate

(Date)

TO \_\_\_\_\_

This is to certify that the following has been taken away for examination in accordance with the law relative to supervision of foodstuffs.

- 1. Items:
- 2. Quantities:
- 3. Place taken:
- 4. Date taken :
- 5. Inspector :
- 6. Reason for taken;

Form No. 2

(Date)

of Aquatic foodstuff inspection report for the month of \_\_\_\_\_.

TO:

FROM: Director of \_\_\_\_\_ Health Office

Inspector \_\_\_\_\_

Results of inspection

Name and address of inspected person:

Inspected items:

Grade of freshness:

Added materials:



Harmful materials:

Grade of sterilization:

Remarks:

Form No. 3

(Date)

Report on abandoned aquatic foodstuff

TO: Governor of Ehimeken

FROM: Director of \_\_\_\_\_ Health office  
Inspector \_\_\_\_\_

We take the liberty to report to you on the above subject as follows:

Name and address of abandoner:

Abandoned items and quantities:

Reason for abandonment:

Form No. 4

Ehimeken

score-card on inspection of aquatic product processing factory.

Address of operator :

Name of operator :

Shipper of material:

Name of manufactured article:



|                                      |                | (Date) |
|--------------------------------------|----------------|--------|
| Daily output                         |                |        |
| Item to be inspected                 | Assigned marks | (Date) |
| (A) Construction                     | 20             |        |
| Site & drainage                      | (4)            |        |
| Ceiling & sides                      | (2)            |        |
| Lighting & ventilation               | (6)            |        |
| Water-closet                         | (4)            |        |
| Store & ice-box                      | (4)            |        |
| (B) Arrangements for                 | 20             |        |
| Water supply                         | (5)            |        |
| Hand washing                         | (2)            |        |
| Draining                             | (3)            |        |
| Rodent & fly prevention              | (10)           |        |
| (C) Administration                   | 50             |        |
| Machines & implements                | (10)           |        |
| Infection prevention                 | (5)            |        |
| Wiping cloth                         | (2)            |        |
| Freshness of material                | (10)           |        |
| Colouring chemicals                  | (1)            |        |
| Storage of manufactured goods        | (10)           |        |
| (D) Individual sanitation            | 10             |        |
| Health of family-members & employees | (5)            |        |
| Personal cleanliness                 | (5)            |        |
| Total                                | 100            |        |
| Remarks                              |                |        |
| Seal affixed by inspector            |                |        |