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(Compiled by *National Diet Library*)

August 12, 1947

SUBJECT: Emergency Medical Supply

TO : Chief of Health Center

FROM : Chief of Ehime Ken Public Health Dept.

In view with many outbreaks of dysentery, the Prefectural Public Health Dept. decided to distribute sulfadiazine and sulfathiazole for the treatment of dysentery cases. It is desired that chiefs of health centers would cooperate with us in control of dysentery, and notify the private doctors of availability of sulfadiazine on the emergency occasion.

SUBJECT: Procedures as to how to obtain sulfadiazine on the emergency occasion.

Private doctors needing sulfadiazine must apply to the health center for the emergency medical supply, showing the detailed data as to the patients' clinical signs. Recall that it is imperative to submit the report on the outbreak of dysentery from private doctors to the health center on each occasion.

Health center chief will issue the certificate of the emergency medical supply on his judgement. Private doctors can get the medicine at the medicine supply shops designated by the Prefectural Health Dept. wherever they show the above certificate.

It is also imperative that private doctors submit the report on the patients given sulfadiazine in strict accordance with the form shown by the Prefectural Public Health Dept.

REPORT ON PATIENT GIVEN SULFADIAZINE

Doctor's Name _____

Patient's Name _____ Age _____

Date of report on outbreak : _____

Short medical history

D Date (1st day) (2nd day)

Dosage

Temperature
(Highest)

Frequency of
passage

Findings on
stools

Caution

1. This emergency medicine should be used only for dysentery patients.
2. It is the responsibility of Health Center Chief to exercise the close supervision over whether the medicine is used with justice or not.
3. It is imperative to send the monthly report from the medicine supply shops to the Prefectural Public Health Dept.

Press

(NANKAI-TIMES: June 13 1947)

SUBJECT: Penicillin Output Increases 50 Fold.

The penicillin industry in Japan is now going to enter into the stage of mass-production. Its output increased approximately fifty fold over last year. Production during April reached 265,050,000 units as compared to only 5,010,000 units in June last year.

The number of laboratories engaged in producing penicillin increased to 25 with participation of 3 more companies in this field of work in the latter part of last month.

The Toyo Rayon Company is now studying the installation of 200 litre tanks for carrying out mass production. It is believed that the nation's monthly production will attain the figure of 3-Billion units by the end of this year.

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Medical Supply Production (19)

On the Effectiveness of "Tomi-Pepton" to
the Culture of Various Kinds of Bacteria

TOMIYAMA Tetsuo
Professor of Chemistry of Fishery Product
At the Faculty of Agriculture of
Kyushu University

I. INTRODUCTION

It has intensively been studied during the time of War II to prepare the culture media for bacteria by the use of fishes as its material. Success was finally made in getting a mixture of pepton and amino acids by subjecting fishes to autolysis under a certain condition. It has been found that this specific preparation, named as "Tomi-Pepton" is very rich in ingredients promoting the growth of bacteria. It is quite a striking fact that just a single solution of "Tomi-pepton" without adding anything else is very effective to culturing diphtheria bacillus and hemolytic bacteria which are not able to grow on the ordinary culture media. It is further being noticed that the formation of penicillin increases in appreciable amount when penicillium No.233 be cultured with "Tomi-pepton" in contrast to the usual commercial pepton.

The present paper deals with the general description of "Tomi-pepton" and with its effectiveness to the growth of numerous bacteria. This work has been carried out with the cooperation of bacteriological laboratory at Faculty of Medicine of Kyushu University.

II. General Description of "Tomi-pepton"

The "Tomi-pepton" can be obtained by subjecting fish as a whole to the autolysis at an appropriate acidity and temperature. The powdered preparation contains in average 5% moisture, 12% nitrogen, and 9% ash. It is mainly composed of pepton and amino acids. The forms of nitrogen are as following.

	%
Protein- and Metaprotein- N	1.9
Protease- N	11.8
Pepton -N	20.4
Subpepton -N	26.0
Amino Acids -N	39.9

III. Results of Growth of Bacteria on "Tomi-pepton"

1. Culture Media:

- a) 2% "Tomi-pepton"
- b) 1% extractives of bonito ± 1% "Teruuchi-pepton".
- c) 1% Liebig meat extract and 1% "Teruuchi-pepton".

2. Species of Bacteria used for the Test:

- 1) *B. coli communis*
- 2) *Staphyl. pyogenes aureus*
- 3) *B. proteus vulgaris*
- 4) *B. subtilis*
- 5) *B. pyocyaneus*
- 6) *Wasservibrio commae*
- 7) *B. paratyphi A*
- 8) *B. paratyphi B*
- 9) *B. typhi*
- 10) *B. dysenteriae Shiga*
- 11) *Coryn. diphtheriae*
- 12) *Streptococcus hemolyticus*

A. Followings are the results of the growth on liquid media:

Species of
bacteria

A. Followings are the results of the growth on liquid media:

Species of Bacteria	Kinds of Culture media	Turbi- dity	Indol reaction	
			Kitasato Salkowski	Prings- heim
B. coli	a)	##	±	+
	b)	+	-	+
	c)	+	-	+
Staphyl. aureus	a)	+	-	-
	b)	##	-	+
	c)	##	-	+
B. proteus	a)	+	-	+
	b)	+	-	+
	c)	+	-	+
B. subtilis	a)	+	-	-
	b)	+	-	-
	c)	##	-	-
B. pycyanus	a)	##	-	-
	b)	##	-	-
	c)	##	-	-
B. nyo Coryn. diph- theriae	a)	##	-	-
	b)	-	-	-
	c)	-	-	-

It has been noticed that *B. pycyanus* cultured on "Tomi-pepton" forms pycyanin in a remarkable quantity not comparable to the control media. When cultured on "Tomi-pepton", indol reaction was much more distinct compared to the other media due to the pale coloration and high tryptophane-content of "Tomi-pepton".

B. Followings are the results of growth of bacteria at 37° and 24 hrs-period on agar-plate culture media.

Species of bacteria	Kinds of culture media	Density of Growth	Largeness of colonies	Thickness of colonies	Order of Superiority
Wasser-vibris commae	a)	++	+++	no difference	1
	b)	+	+		3
	c)	+	+		2
<i>B. paratyphi</i> A	a)	+++	+++	No difference	1
	b)	+	+		3
	c)	+	+		2
<i>B. paratyphi</i> B	a)	+++	++	+++	1
	b)	+	+	+	3
	c)	+	+	+	2
<i>B. typhi</i>	a)	+++	++	+++	1
	b)	+	+	++	2
	c)	+	+	+	3

B. dysenteriae	a)	++	++	No	1
	b)	++	±	differ-	3
	c)	++	++	ence	2

It is to be pointed out that egg white is ordinarily needed to clarify the agar media while "Tomi-pepton" can be used without such process of clarification.

C. Detection of vibrio commae

When 5 cc of 2% "Tomi-pepton" are inoculated with *Vibrio commae* in so tiny amount as 1/100,000 of a platinum-loopful quantity of the bacteria, distinct turbidity and cholera-rose reaction appeared after 5-6 hrs' incubation. However, in the control experiment using Liebig meat extract, the reaction was positive only after 24 hrs' incubation. Thus, it will eventually be an outstanding contribution to the prevention of infectious cholera-disease that "Tomi-pepton" is certainly able to facilitate the early detection of *Vibrio commae*.

D. The culture of certain pathogenic bacteria:

(1) The culture of *Coryn. diphtheriae*.

The rate of growth of *Coryn. diphtheriae* is two to three times better on "Tomi-pepton" than on "Löffler's" or "Martin's" media specific for this bacteria. The following points are worthy to be mentioned.

- a) The 24 hrs' incubation after inoculation to 2% Tomi-pepton is enough to obtain a fairly good formation of membrane on the liquid media.
- b) The positive activity of formotoxoid formed by inoculation in 2% Tomi-pepton was clearly observed in dilution of 1/100,000, and doubtful activity in dilution of 1/200,000.
- c) The voltin of this bacteria grown on Tomi-pepton can clearly be observed without fail after staining. Therefore, it will be quite feasible by the use of Tomi-pepton to identify *Coryn. diphtheriae* and to efficiently manufacture the formotoxoid.

(2) The culture of hemolytic streptococcus

It is striking that this bacteria which is only capable to grow on blood-agar medium can grow quite normally on a simple 2% solution of "Tomi-pepton".

(3) The culture of *Mycobacterium tuberculosis*:

A good result was noticed when monosodium glutamate of "Oka)Katakura" medium be replaced with "Tomi-pepton".

LV SUMMARY

1. Tomi-pepton medium is far superior to the usual one in culturing various kinds of bacteria judging from the magnitude of their colonies on agar-plate and turbidity of liquid culture media.
2. The formation of pyocyanin by *B. pyocyaneus* cultured on Tomipepton was very rapid and remarkable.
3. Indol reaction on the Tomi-pepton medium inoculated by *B. coli*, *Staphyl. aureus*, and *B. proteus* was marked and can easily be detected due to the pale coloration of "Tomi-pepton".
4. The liquid medium of "Tomi-pepton" gives easily perceptible positive cholera rose reaction at 3-6 hrs' period after inoculation of *Vibrio comma* in quantity of 1/100,000 of loopful bacteria.
5. The Tomi-pepton can be used with good result instead of monosodium glutamate in the culture of *Mycobacterium tuberculosis*.
6. *Coryn. diphtheria* can grow on a simple 2% solution of Tomi-pepton with two to three times better growth compared to Löffler's or Martin's culture media. The volutin of the bacillus grown on Tomi-pepton can be identified without fail on standing.
7. The followings may be pointed out as outstanding characteristics of Tomi-pepton in practical use.
 - a) It is feasible to detect the turbidity, the formation of pigment and the chemical test of the metabolic product of bacteria due to the pale coloration of the media.
 - b) A simple 2% solution of Tomi-pepton can be used for the culture of bacteria without the addition of extractives and sodium chloride.
 - c) A simple filtration is suffice to clarify the media, and no turbid matter forms on the sterilization.

A STUDY ON THE PREPARATION OF AN IDEAL
SUBSTITUTE FOR MOTHER'S MILK

- T. Tomiyama: Prof. of Chemistry of Fishery Products at Faculty of Agriculture, Kyushu University.
 T. Sugihara: Formerly Lecturer at Faculty of Agriculture, Kyushu University.
 M. Enjoji: Prof. of Pediatrics at Faculty of Medicine, Kyushu University.
 I. Chin: Director of Infant's Hospital at Faculty of Medicine, Kyushu University.
 K. Ando: Research-fellow in Infant's Hospital at Faculty of Medicine, Kyushu University.

Due to a lack of milk and milk product, it is now very difficult to maintain the nutrition of sucklings normal. Without using milk or milk product, never success has been made in preparing an ideal substitute for mother's milk. So it is a great desire to prepare in a large quantity an ideal substitute by making use of foodstuffs other than milk. An attempt has been made to prepare an ideal substitute by adopting certain foods or food components which are rather abundant in Japan.

The present paper deals with a success in preparing without milk a real substitute, the nutritional value of which has been determined on albino rat as well as sucklings. In this paper, the present preparation of the substitute may simply be called "Nutron".

I. Materials and Method of Preparation, and
Chemical Composition of "Nutron"

1. Materials

	Grams	% components to be used
Wheat flour	1000	80
Pepton prepared from fish	100	8
Vegetable oil and butter	75	6
Liver oil of high vitamin	2 capsule	-- (10,000 I.U.)
Yeast	50	4
Calcium lactate 7 and sodium chloride 10	17	1.4

2. Method of Preparation : Wheat flour, vegetable oil, butter, liver oil and yeast are well mixed with a suitable quantity of warm water. The mixture, after standing several hours, is steamed or baked, then dried, and further pulverized. To this powder an adequate amount of powdered pepton is intimately admixed, giving the substitute "nutron" in powder form.

The above processes aim at emulsifying oil and dextrinizing wheat flour. Thus "nutron" is entirely composed of easily digestible nutrients, i.e., pepton, oil-emulsion, and dextrin.

3. Chemical Analysis of "Nutron" : A chemical analysis gives 4.2% moisture, 14.0% protein, 5.8% fat, 3.7% ash, 62.3% carbohydrate.

II. Nutritional Value of "Nutron"

A. Feeding Experiments on Albino Rats.

Albino rats (same litter) raised by "nutron" showed quite regular and excellent growth (Fig. 1). Up to 150 g in body weight, average increase amounted to 2.7-3.4 g per day at 20% protein level and 2.3-2.8 g per day at 14% protein level.

The digestibility of total solid has been determined during nine days. The results are shown in table 1. The average value for digestibility has been found to be 93.0%.

B. Nursing Experiments on Sucklings.

Several preliminary preparations of "nutron" were tested on six sucklings from Nov. 1944 to May 1945. The experiment was not able to carry out long enough to get a clearcut results owing to the fact that difficulty was experienced in drying process and further it was hard to get materials for preparing "nutron" due to the food-crisis. Here description will only be made of the experiments on two sucklings nursed for two months with "nutron" in powder form.

One suckling A is male and five months old. His nutriment, powdered milk, was gradually replaced during 10 days with "nutron". The other suckling B is male and three months old. He had been nursed exclusively with mother's milk which was replaced during 3 days with "nutron".

The kinds of nutriment, amount of the nutriment ingested, body weight and number of excretion of feces are given in table 2. The following points need to be mentioned. 1) Appetite: the suckling A seemed to like to drink "nutron" even without sugar. In suckling B no difficulty was experienced in replacing mother's milk with "nutron" within three days. The appetite for "nutron" has been observed throughout the experiment to be very good except when suckling B was suffered from the epidemic influenza. 2) Feces: quite normal except slight diarrhea when suffered from the epidemic influenza. 3) Skin: normal. 4) Growth: normal (Fig. 2).

The digestibility and nitrogen balance of the nitrogenous constituent have been determined. The results are given in table 3. It will be seen that the nitrogenous constituent of "nutron" was as much utilized as that in mother's milk. In suckling B, the protein-content in serum has been found to be normal.

As to the resistance to infection, it must be mentioned that the suckling B was infected by influenza which was just prevalent in the infants' hospital. However no particular week resistance has been noticed in two sucklings under examination compared to the other ones in the hospital.

III. Summary

Without using any milk or milk product, no ideal substitute for mother's milk has yet been prepared. It can be emphasized that as an ideal substitute for mother's milk the present preparation "nutron" may be the first one so far as is now known.

The characteristics of "nutron" can be pointed out as follows. 1) The materials for "nutron" especially fish and wheat are common, rather abundant, and cheap resources in Japan. 2) All the components are changed into easily digestible form, i.e., pepton, oil-emulsion, and dextrin. 3) "Nutron" may have many points which meet the taste of sucklings, since they like to drink it even without sugar. 4) The nutritive value of "nutron" has been ascertained to be complete by feeding albino rats as well as nursing several sucklings.

The experiments have shown that by the use of "nutron" it is no longer difficult to keep normal the nutrition of sucklings few months old even without having any milk or its product. It is eagerly hoped that many sucklings will soon be rescued from their malnutrition by the abundant supply of "nutron".

Addendum: Quite recently a nursing trial is being made to start to give "nutron" to a baby immediately after birth without giving mother's milk at all. The response to "nutron" is coming out excellent. This will be reported later on.

Table 1 Digestibility of "nutron"

		Date: April									
No. of rat		12	13	14	15	16	17	18	19	20	
Anutron" ingested	No.15	14.4	15.4	16.3	16.0	18.3	17.0	17.2	18.1	18.1	
	No.35	14.1	15.1	16.0	16.9	15.9	16.2	18.2	17.5	18.8	
	No.20	14.1	15.1	16.0	13.1	14.7	14.2	15.3	16.3	17.5	
Feces excreted	No.15	1.0	1.0	1.0	1.3	1.3	1.3	1.3	1.3	1.2	
	No.35	1.2	1.1	0.7	1.3	1.0	1.3	1.5	1.3	0.9	
	No.20	1.3	1.1	1.1	1.4	1.0	1.1	1.3	0.9	0.9	
Diges- tibility	No.15	93.0	93.5	93.7	92.0	92.8	92.5	92.5	92.8	93.3	
	No.35	91.5	92.8	95.1	92.3	92.7	92.2	91.7	92.6	95.1	
	No.20	91.0	92.8	93.0	89.5	93.3	92.5	91.5	94.5	94.5	

Table 2 Growth of Sucklings

No. of suckling	Kinds of nutrition	Days after birth	Period of Expt. (day)	Increase in body wt. total	Increase in body length (cm/month)	Calorie per day total	per Kg.	average no. of excretion of feces per day
A	Milk powder	121	30	310	10.5	634-644	114-127	1.2
	"Nutron"	153	73	880	12.1	510-805	103-143	1.4
B	Mother's milk	80	.5	150	30.0	700-826	109-131	2.0
	"Nutron"	85	73	1300	17.8	332-979	48-140	2.2

Table 3 Digestibility and Nitrogen Balance of Nitrogenous Constituent in "Nutron"

Age in month	Date of test	Kind of Nutrient	N ingested (g)	N out-put in feces	N out-put in urine	N absorbed (g)	N digestibility (%)	N deposited (g)	N deposited in % of ingested
♂ A	5	27, 28 Jan. Milk powder	4.99	0.69	2.28	4.30	86.1	2.02	40.4
	6	27, 28 Feb. Nutron	4.89	0.92	1.28	3.97	81.2	2.69	55.0
	7	19, 20 Mar. Nutron	3.84	0.36	1.24	3.48	90.7	2.24	58.3
♂ B	3	30, 31 Jan. Mother's Milk	2.16	0.41	0.39	1.75	81.0	1.36	62.9
	4	11, 12 Feb. Nutron	3.98	1.06	1.22	2.92	73.4	1.70	42.7
	5	21, 22 Mar. Nutron	3.84	0.67	1.54	3.17	82.7	1.63	42.4
Control	♂ I 4	22 Jan. Milk	4.90	0.34	2.72	4.56	93.1	1.84	37.6
	♀ II 6	26 Jan. Milk & lactose	4.90	0.28	2.28	4.62	94.3	2.34	47.8
	♂ III 7	13, 14 Feb. Milk & cereal	2.48	0.30	1.08	2.18	87.8	1.10	44.3
	♀ IV 6	15, 16 Feb. Milk & cereal	2.48	0.25	0.85	2.23	90.0	1.38	55.7
	♂ V 9	9, 10 Feb. Special food for infant (Daji-shou)	4.32	2.58	1.23	1.74	40.3	0.51	11.8

body wt.
in
grams

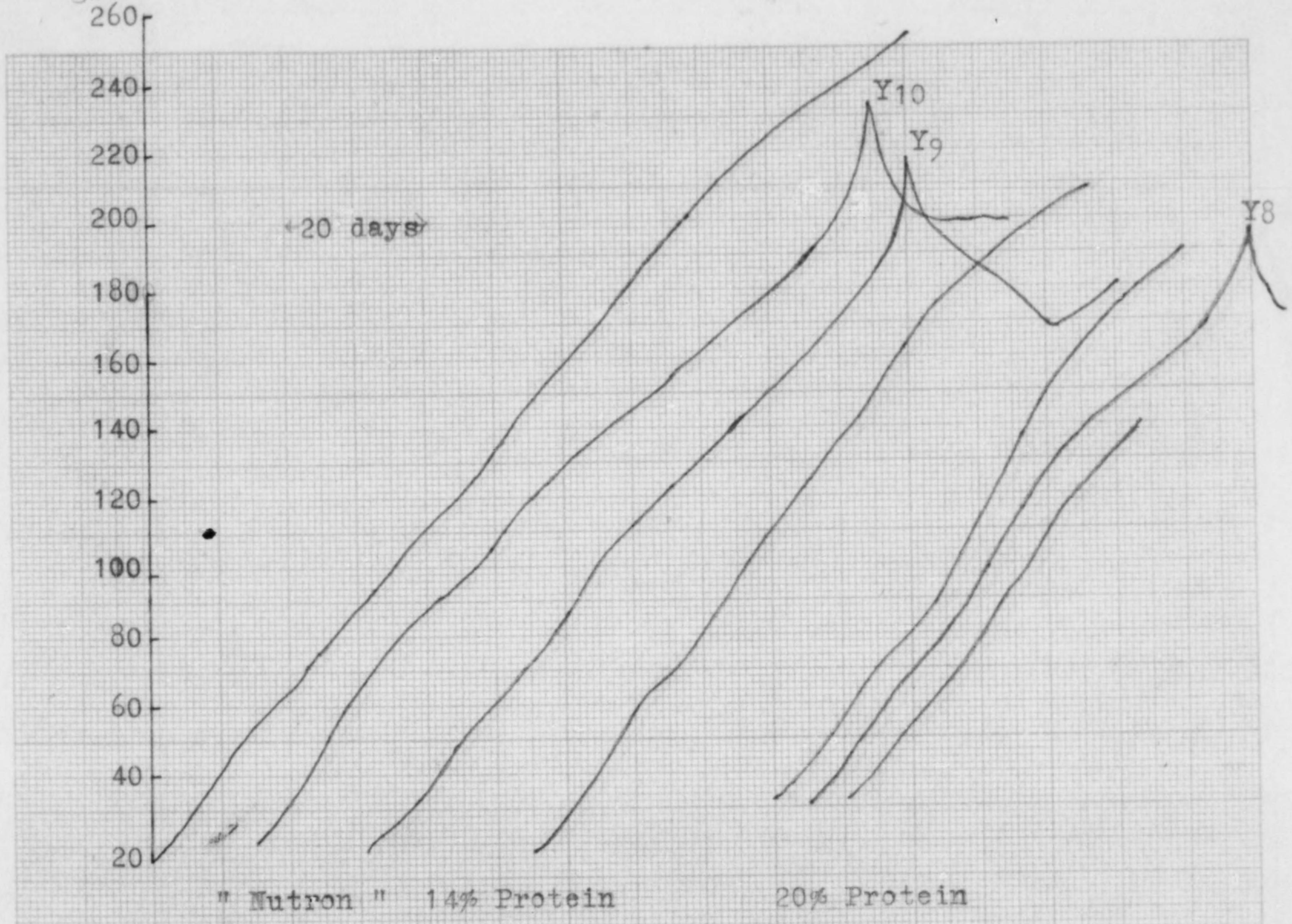


Figure 1 Growth of Albino Rats

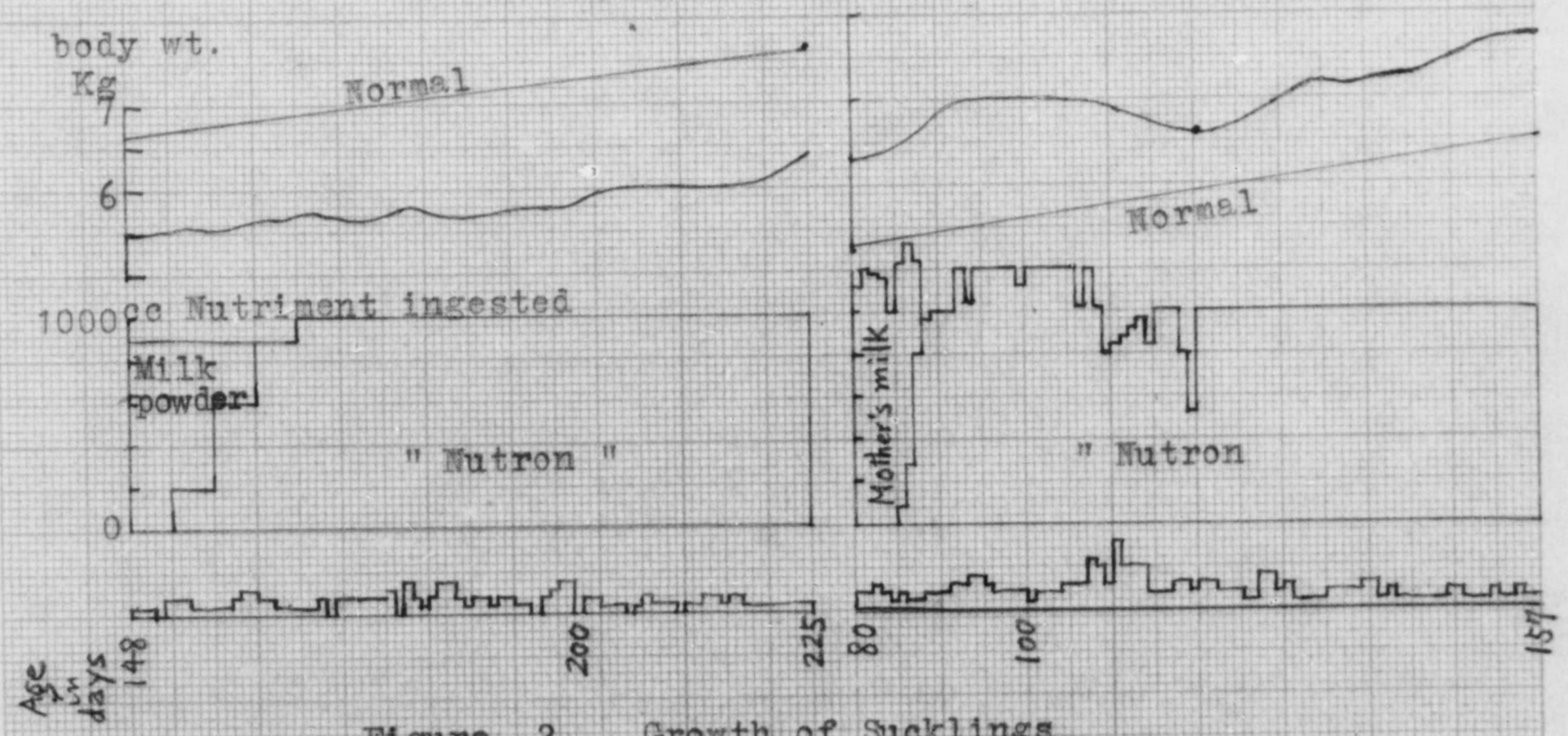


Figure 2 Growth of Sucklings

Materials required for the Preparation of "Nutron"

Average quantity of "Nutron" per Infant, per Day	160	g
" " " per 1,000 Infants, per Day	160	Kg
" " " per 1,000 Infants, per Month	4,800	Kg

No.

Materials	Monthly Need
Wheat flour	3,200 Kg
Sugar	800 "
Vegetable Oil	200 "
Butter	100 "
"Tomi-Pepton"	680
Yeast	120
Calcium carbonate	28
Vitamin A and D (Vitamin oil concentrate)	2

2000 babies now on Nutron -
to last 3 mos.

Nutron 170 Cal per 100 gm -
Pepton 300 Cal per 100 gm -

Sardine - fresh -

-les workers-

2 months

P E N I C I L L I N

ITS

PRODUCTION AND RESEARCH

NIHAMA WORKS

NISSIN CHEMICAL CO., LTD.

Penicillin production program and outline of research projects
performed of the Nihama Works, Nissin Chemical Co.

January 1947

A. Introduction :

Preliminary research work of penicillin preparation was commenced on February 1944 and substantial work by March of 1946.

(1) On 15 August 1946, joined the Penicillin Committee established under the sponsorship of Major Jordan and other GHQ officials.

(2) On 15 to 17 of December we had the honour of attending Dr. Foster's lecture, subject "Penicillin production in the United States", taking place at the Welfare Ministry. Professor's lecture may be summed up to the following meaning: "It required three years for the United States to succeed on the submerge culture method. And I think, for this method to be available in Japan at least three years is necessary. The production of penicillin of this country up to October 1946 averages only 22,500,000 units per month while the amount required to treat only serious tuberculosis cases calls for 2,100,000,000 units per month in average. (According to the statistics announced by the Welfare Ministry.) Drastic steps must be taken in order to meet this demand and make way for the large-scale production in the least time possible. Consequently the aim of GHQ and the Japanese Welfare Ministry is to encourage the rapid increase of output of penicillin by the surface culture method and on the other side to cooperate willingly to the utmost in the line of research and technical mastering by the submerge culture method." In addition, the Japanese Welfare Ministry has decided in order to obtain permission for penicillin production, it is required that the factory must have a capacity of over 500 L/day (60,000,000 to 12,000,000 units)

(3) On 9th December 1946, in room No.610 of the Public Welfare Section of GHQ a conference concerning penicillin production was assembled. The attending members :

GHQ Prof. Dr. Foster
 Colonel Willow
 Major Sprague and others

Japanese side

Commerce and Industry Ministry
Welfare Ministry
Chemicals Controlling Association
Representatives of the principal chemical companies
invited by GHQ.

Our Nissin Chemical Co., Ltd. was bestowed with the honour of the invitation. The summary of the speeches of Prof. Dr. Foster, Major Sprague and others were to the following meaning :

Dr. Foster : The penicillin necessary for this country must be self supplied. The United States will not supply Japan with it, but there will be no bounds as to technical and other assistances necessary. Dr. Foster will be responsible for the technical advises and Major Sprague will assist in the field of raw materials, fund and legal advices.

Large scale production by the surface culture method is impossible, and consequently it must be substituted by the submerge culture method. Production by this latter method is of a nature that it can be rightly named as a heavy chemical industry, hence it is not a task to be tackled by various small companies as is the current situation in this country. This is the reason of our inviting by name today, the 10 and over leading chemical companies of this country. I ask for the immediate decision of each company whether they will take up this job. And to those companies that have decided to adopt the submerge culture method, utmost assistance by GHQ in all

fields may be promised.

(2) Major Sprague : Without the efforts of large companies, the success of penicillin industry is impossible. If, in order to shift to large scale production by the submerge culture method, exemption from reparation, mollification of the anti-trust law and other effecting items are necessary, I will do my best to help you on the way. If you may have difficulties in obtaining funds because of being a restricted concern, you will be assisted. If you have any other troubles, please consult Major Sprague. If there is any raw material inavailable in this country I will prepare and have it delivered to Japan. It has already been arranged in the States to supply you with amylacetate.

(4) On the 19th of December 1946, in response to the order of GHQ, a meeting was held under the sponserhip of the Commerce and Industry Ministry, in the conference rooms of the Chemicals Association. And at that occassion each company was demanded to announce its attitude towards its resolution of taking up the production in response to the signification of the meeting of 9 December.

Our Nissin Chemical Co., Ltd., gave the following answer : In the near future substantial production by the surface culture method will take place. Concerning the penicillin production by the submerge culture method, research work and preparation for pilot plant experiment is being carried out.

B. Penicillin production program

Alongside with the commencement of work on pilot plant and actual production by the surface culture method, investigations will be started on the research and pilot plant experiments utilizing the submerge culture method.

Detailed explanation of the plan :

1) Operation method :

Please refer to attached flowsheet diagram.

2) Capacity :

In the first stage the capacity is to be 50 L/day (i.e. from 200 to 250 of one liter Erlenmeyer flasks will be used per day.) which will further be expanded to 100 L/day.

3) Construction plan of the pilot plant :

Location : A part of the former (5 T/month) synthetic rubber plant will be used. By its selection within this factory, it was contemplated as most suitable for carrying out the production and research work owing to its isolated position on the farther end of the island, thus decreasing the possibilities of being effected by the dirty air.

Degree of progress of the construction : (up to present)

Buildings	:	ca. 70 % completed
Machinery	:	under making
Erection	:	not yet started

Estimate as to date of its completion :

The former schedule dated it as March, but owing to the time required for the application for the release of the reparation buildings to be approved, the completion will be behind time.

4) Facilities :

Please turn to chart No.1.

(The rooms are numbered in compliance with chart No.1.)

(1) Preparation room :

12.6m X 20m Area 252 ^{square} ~~cubic~~ m.

Accommodated with facilities for washing bottles, preparation of culture media and sterilizing. (Either by steam or by heat.)

(As this pilot plant was projected for a short term, the whole process is to be manipulated by hand.)

(2) Inoculation room :

3m X 5m Area 15 ^{square} ~~cubic~~ m.

The walls will be coated with a layer of concrete and in order to maintain cleanliness, facilities for frequent washing will be installed.

Sterilized culture media bottles (one liter Erlenmeyer flasks) will enter from one window and after being inoculated will be passed out from another window.

(3) Culture room :

4.5m X 12.1m Area 54.5 ^{square} ~~cubic~~ m.

Ceiling and the side walls will be made thermoinsulated by filling with saw-dust. In the interior, shelves will be attached capable of holding 3,500 culture bottles at a time.

In order to maintain the room temperature at a constant 25 degree Centigrad; in summer, air is cooled by cold brine solution and in winter warm air heated by steam will be blown in. It will be connected by different windows with the culture and assay rooms respectively.

(4) Assay room :

4m X 5m Area 20 ^{square} ~~cubic~~ m.

(5) Machine room :

4.5m X 12.6m Area 56.7 square m.

The following machineries will be installed :

(") Refrigerator	200HP	200,00 KCal/hr	1 set
Air heater & cooler	(Under construction)		1
Blower	3 HP	60 m ² /min	2
(") Transformer	3 phase	150 Kva	1
(") " "	1 phase	20 Kva	1
(") Switch board			1

Remarks: The items with the mark (") are listed in the inventory as reparation objects.

(6) Electric boiler room : (Pump room attached)

8m X 10.6m Area 74 square m.

To be newly constructed on the east side of the former synthetic rubber plant building, and following equipments will be installed :

Electric boiler	250KW	1	under making
Transformer	600KVA	1	
Pump (Water)	5HP	1	
Heatexchanger		1	

The steam for the whole process will be supplied from here.

(7) Refining room :

8m X 14.4m Area 115 square m.

(The former butadiene storage room will be used.)

- a) Normal temperature room 8m X 8m 64 m²
- b) Low temperature room 36
- c) Refrigerating room 6

- a) Normal temperature room : The process of filtration of the culture medium, adsorption by active carbon, extraction by acetone and evaporation of acetone,

will be carried out in this room.

This room will be equipped identical with ordinary laboratories, and absorption and extraction tanks with cooling jackets are to be installed.

b) Low temperature room :

The room temperature must be constantly maintained under 10 degree Centigrad. The process to be performed in this room ; The aqueous solution from which acetone is removed by evaporation, is extracted with either ether or amylacetate. And this is further treated with a buffer solution to extract the product. And lastly this is dried under refrigerated condition and made into a finished product. By consideration of manipulation efficiency and in order to maintain most suitable conditions the room is thermo-insulated by installing double walls filled with saw-dust and temperature regulated air is supplied. Brine tanks of minus 5 and minus 50 degree Centigrade are installed, the former for the general cooling and latter for use for trap off the process of drying by refrigerating.

c) Refrigerating room :

Its use for refrigerating raw materials for culture mediums, such as; yeast, worked fishery products, penicillin intermediate refined solutions and storage of the finished products.

It will be thermo-insulated by double walls, filled by saw-dust. The room temperature will be maintained at 0 - 50 degree Centigrade.

5) List of principal machineries.

<u>Item</u>	<u>Size & Capacity</u>	<u>Unit</u>	<u>Purpose</u>
1. Dry heat sterilizer	1.5mX1.5mX1.4m box-type	1	coal-gas heated
2. Steam sterilizer	1.5mX1.8mL horizontal-cylinder	1	
3. Air heating & cooling appat.	1mX1mHX0.6m tube-type	1	heating and cooling culture room
4. Refrigerator	200,000Kcal/hr 200HP	1 (")	for refrigerating refrigerator room, culture room & refining room etc.
5. Air cooler	1.0mX1.0mX1.4m tube type	1	for cooling the refining room.
6. Blower	3HP 60m ³ /min. 30cm/mH ₂ O	2	for refrigerating.
7. Pipe (air)	310 X 360	40m	" " "
8. Electric boiler	250KW horizontal volume of boiler 1.2mX3m	1	
9. Plunger pump	3"φ 5HP	1	for supplying water to boiler.
10. Heat exchanger	0.6mX1.0m multi-tube type	1	for boiler blow water.
11. Compressor	oil compressor volume 0.7L	1	for pressing and filtering mold.
12. Stirrer	1/2HP 1,000Y.L.M.	3	for culture media & penicillin refining.
13. Vacuum pump	1/2HP Gaede type exhaust 80L/min 0.002mmHg	2	for penicillin refining.
14. Diffusion pump. (oil)	10 ⁻⁶ mmHg	1	for penicillin drying.
15. Brine tank	0.6mX0.6mX1.2m	1	" "
16. " "	0.4mX0.4mX1.2m	1	" "
17. Continuous centrifugal separator	1/2HP capacity 300-500L/hr	2	for preparing culture media & penicillin refining.
18. Transformer	3 phase 150KVA primary 33,000V secondary 220V	1 (")	
19. " "	1 phase 20KVA 2ndary 110V	1 (")	

List of principal machineries. (Continued)

<u>Item</u>	<u>Size & capacity</u>	<u>Unit</u>	<u>Purpose</u>
20. Switch board		1 (")	
21. Pplings		1 set	for water, coal gas, steam and brine.

REMARKS: Items marked with (") are those designated for the reparation purposes as part of the machineries of the synthetic rubber plant, and for its release an application was submitted to GHQ on 30 January 1947.

6) Estimates of research period and amounts of test products to be produced.

Research period : From March 1947 to December 1947.

(This date will undergo a little modification owing to the suspension of the construction of the plant ordered by the Military Government.)

Amount of test products : Products are expected to be turned out from July.

1,200,000 - 2,400,000 unit/day

7) Technicians and laborers.

Technicians : 8

Laboratory assistants : 15

8) Materials.

a) Yeast : This item will be self supplied. At present, we have a producing capacity of 5 Kg per day, which will be increased to 60 - 300 Kg per day after completion of the new yeast plant now under way.

b) Glucose : A part will be self supplied and the residue we must rely on the supply from the outside.

We are accommodated with a facility for producing 200 Kg per day and are prepared with plans for its further expansion, and at present are encountering difficulties in securing methanol for refining yeast. Sufficient amount for carrying out the pilot plant research work are in our heads, but in order to carry out the pilot plant research work by the submersion method, yeast must be supplied from the outside.

c) Raw materials for yeast production: In order to beg the distribution of dried sweet potato and rice-bran,

an application was submitted to the Ehime prefectural office.

d) Aceton : A considerable amount is in stock.

e) Amylacetate, phenylacetic acid and active carbon :

Concerning these items we are expecting their supply thro the Penicillin Association. (The former two items are to imported by the generous favor of GHQ.)

f) Worked fishery products : In the case of large-scale production, we are planning to mix it with yeast. At present the amount available is under investigation.

9) Molds to be used :

Shared from GHQ : No. 1978 B.2. and No.1249 B.21

Japanese molds : G.I., No.233 and No.176.

10) Influence of removal of machineries and buildings for reparation purposes : Concerning the buildings; The plant was planned to be installed in the former synthetic rubber plant by the conversion of a part of its building facilities. Work is being continued after being withheld for 28 days required for obtaining the approval of the Military Government to use these items for penicillin production.

Concerning the machineries of the former synthetic rubber plant: Machineries, which we beg the release from reparation inventories are as following;

Equipments :

1) Refrigerator	200HP 200,000KCal/hr	1 set
2) Transformer	150KVA 3 phase	1
3) " "	20KVA 1 phase	1
4) Switch board		1

B. Program (Estimate) of production in large-scale by the ^{surface culture} submersion method.

- 1) Capacity : 500 L/day by the surface culture method.
(scheduled to shift to the submerge method on the completion of its research work.)
- 2) Commencement of production : Undecided.
- 3) Details of the plan : This producing capacity is to be attained by the expansion or further additional construction of the 50L/day pilot plant experimenting facilities in the former synthetic rubber plant. We are of the estimate that the refining room and the refrigerator will require no further addition.
- a) (The numbers of the following list is identical of those inscribed in chart No.2)
- 1) Preparation room : This will be expanded as described in the chart. Facilities for washing bottles, preparing culture media and sterilizing will be newly installed.
- 2) Inoculation room
- 3) Culture room Scheduled to be newly installed
- 4) Assay room within the synthetic rubber plant.
- 5) Filtrating room : To be newly installed on the west-side of the building.
- 6) & 7) Machinery room : 6) is to be expanded to 7).
Air cooling and heating apparatus and 2 blowers of 3 HP are to be newly installed.
- 8) Electric boiler room : Does not require expansion.
1 boiler of 250 KW capacity will be newly installed.

11) Storage room for raw materials :

4) Relations with reparation : As the expansion will be limited to building facilities in this stage, we hope that there will be no trouble about it as we have obtained the approval of the Military Government to use the 3 buildings of the 5 T/month plant.

C. Plan of the pilot plant research work by the submersion method.

As a primary stage plans have been projected to the capacity of 2 to 8 culture tanks of a volume about 500 liters. We are of the expectation that we might be honoured by the personal instructions of Prof. Foster of OHQ.

D. Plan of production in large-scale by the submersion method.

As this theme is under investigation, it has not developed into a definite plan at present.

Estimates are that at least a few tanks of 50,000 - 100,000 liter capacity must be installed.

Outline of the research work concerning penicillin performed
in the Nissin chemical co., Ltd, Mihama Ehime-ken.

A) Research work of penicillin and penicillin analogous substances. :

Work performed on various penicillin molds of its anti-bacterial strength has rewarded us with two or three strains of practical worth. No investigations have been undertaken on its bacteriological properties.

In order to discover microbes with the ability to produce substances effective against bacillus undestroyed by penicillin, work was devoted in the direction of isolating Actinomyses mold and testing its antibacterial potency. Succeeded in obtaining a few strains of antibacterial potency against bacillus coli, the exact potency of which is yet to be assayed.

B) Research concerning culture media :

Work is being carried out with aims to improve the culture conditions. We have obtained positive proofs that starch, raw sweet potato, raw Irish potato and unrefined glucose can be used as carbonaceous source. And as nitrogenous source; yeast, fish flesh and entrails, may be utilized. Moreover, as it was clarified that autolysate solution made be utilized as material, work is being performed on finding the most suitable condition for its development.

C) Research on the refining method. :

Arrangements of the facilities are being carried out at present on the line of the following process; absorption by active carbon, extraction by acetone, and extraction from the aqueous solution, after the removal of acetone, with ether.

Scheduled to be completed in the near future.

D) Investigations on large-scale production :

In order to set out on the preliminary experiment by the submer-sion method, a shaker was designed and is now under construction.

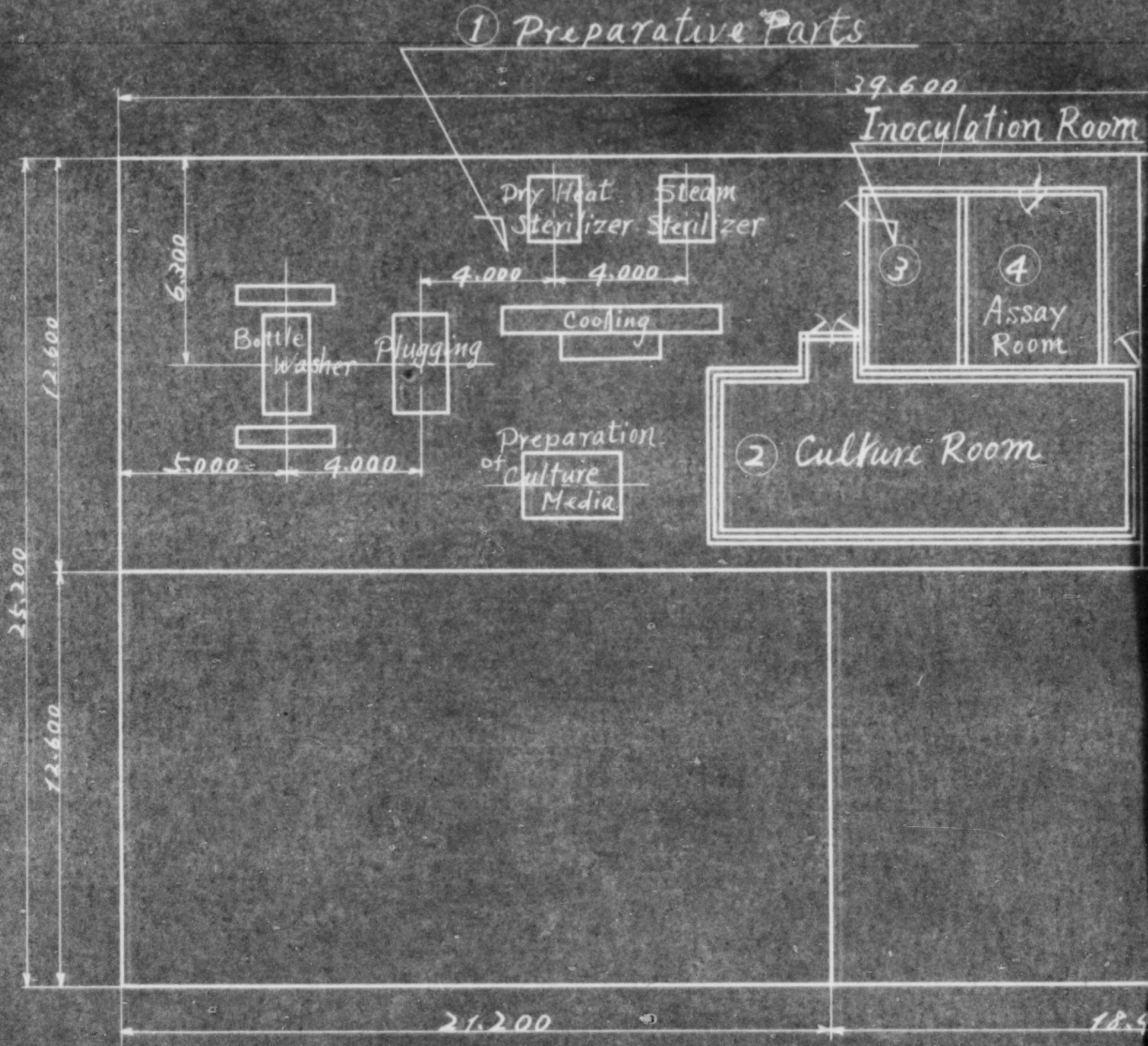
Investigations are being carried out for the construction of the pilot plant by the submersion method.

In addition, By the test of producing penicillin by the Koji method (by adding the yeast autolysate solution to the rice-bran) we obtained a considerable amount, but research is still being carried on.

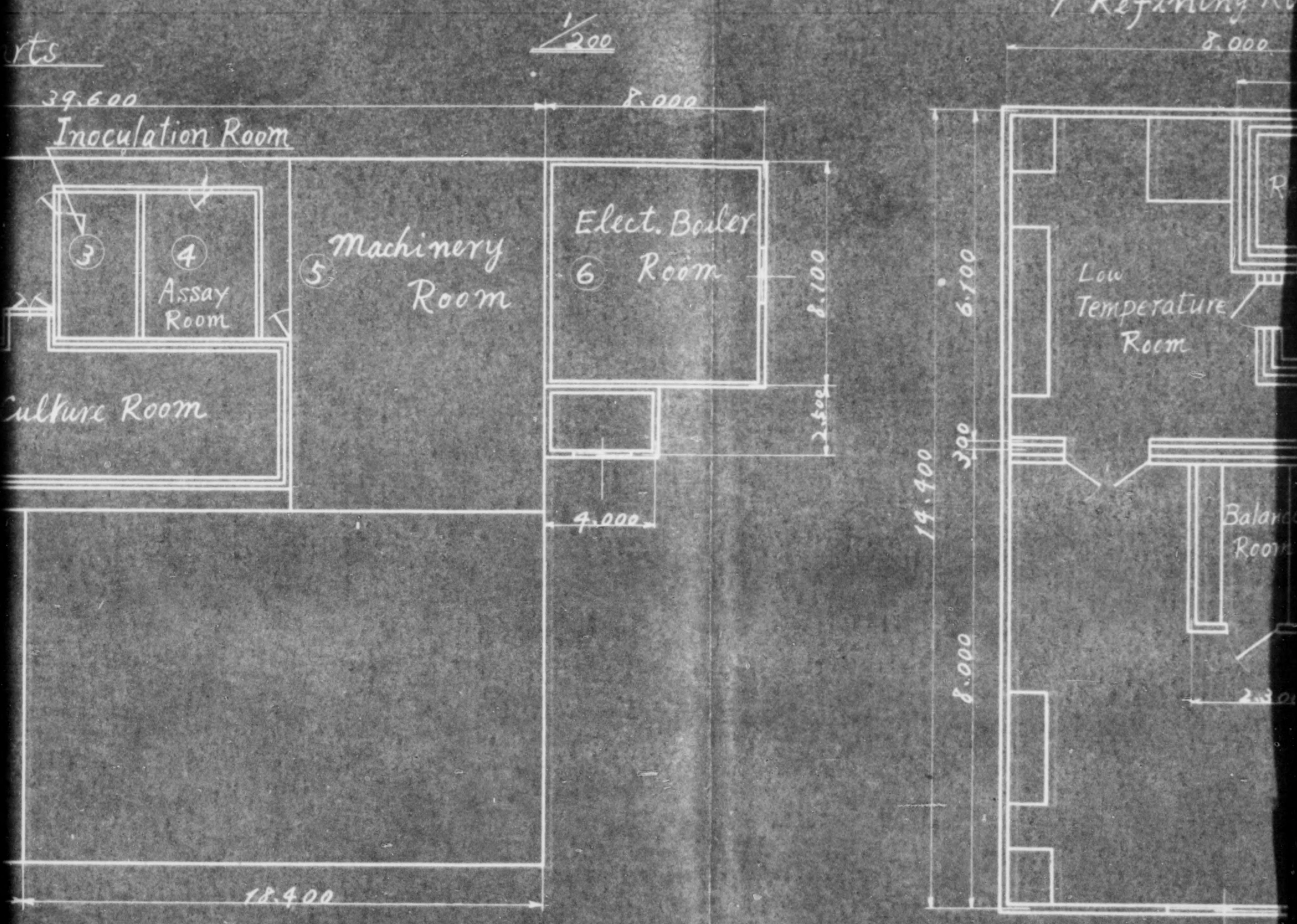
We would like to express our gatitude to the generous favor of GHQ, by whose kindness we were shared through the Penicillin Association, three strains from America, one of which is for submersion culture and others for surface culture.

FIG. NO. 1

Semi Common



Semi Commercial Plant of Penicillin Manufacturing



Manufacturing 50^l/day surface culture

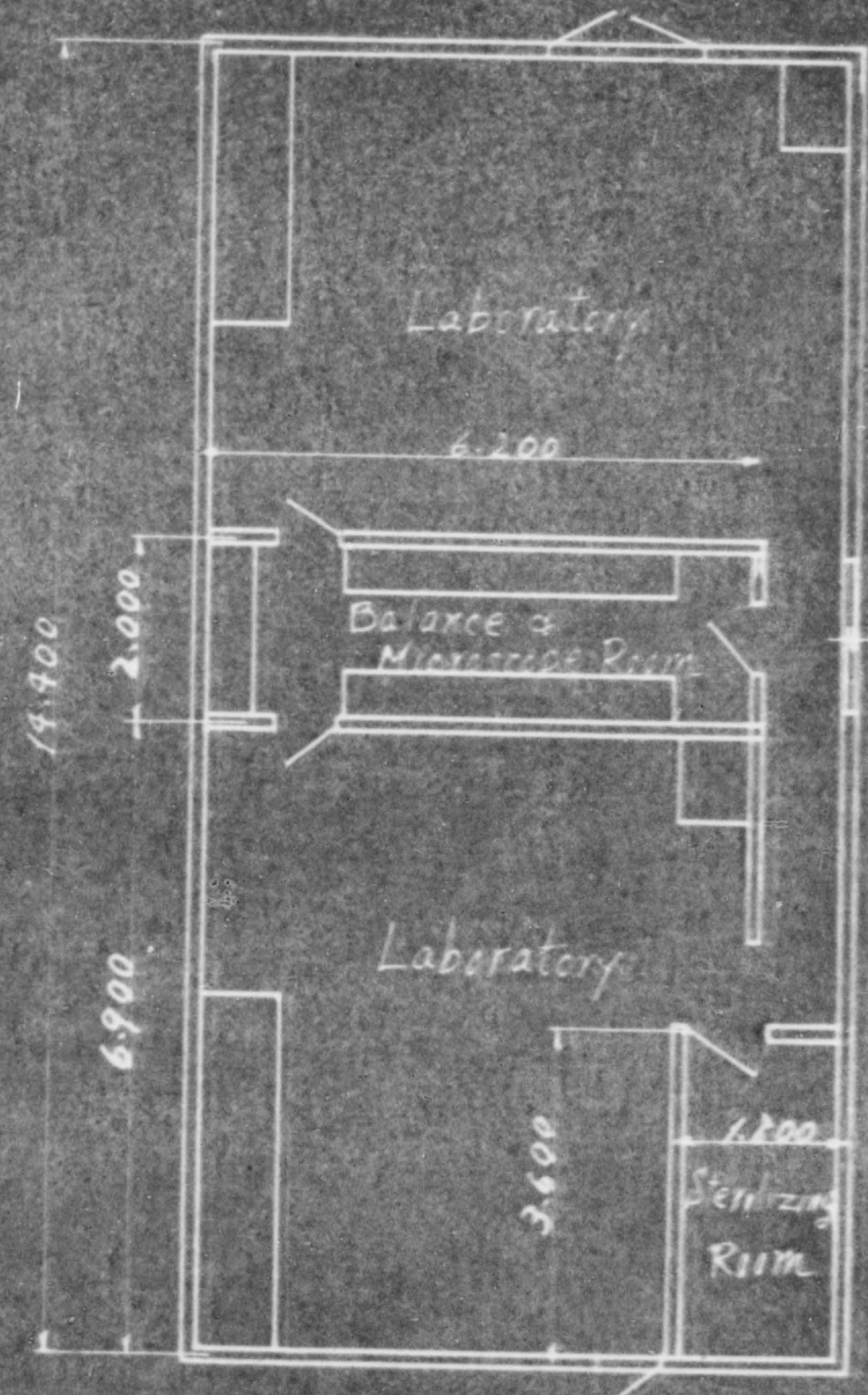
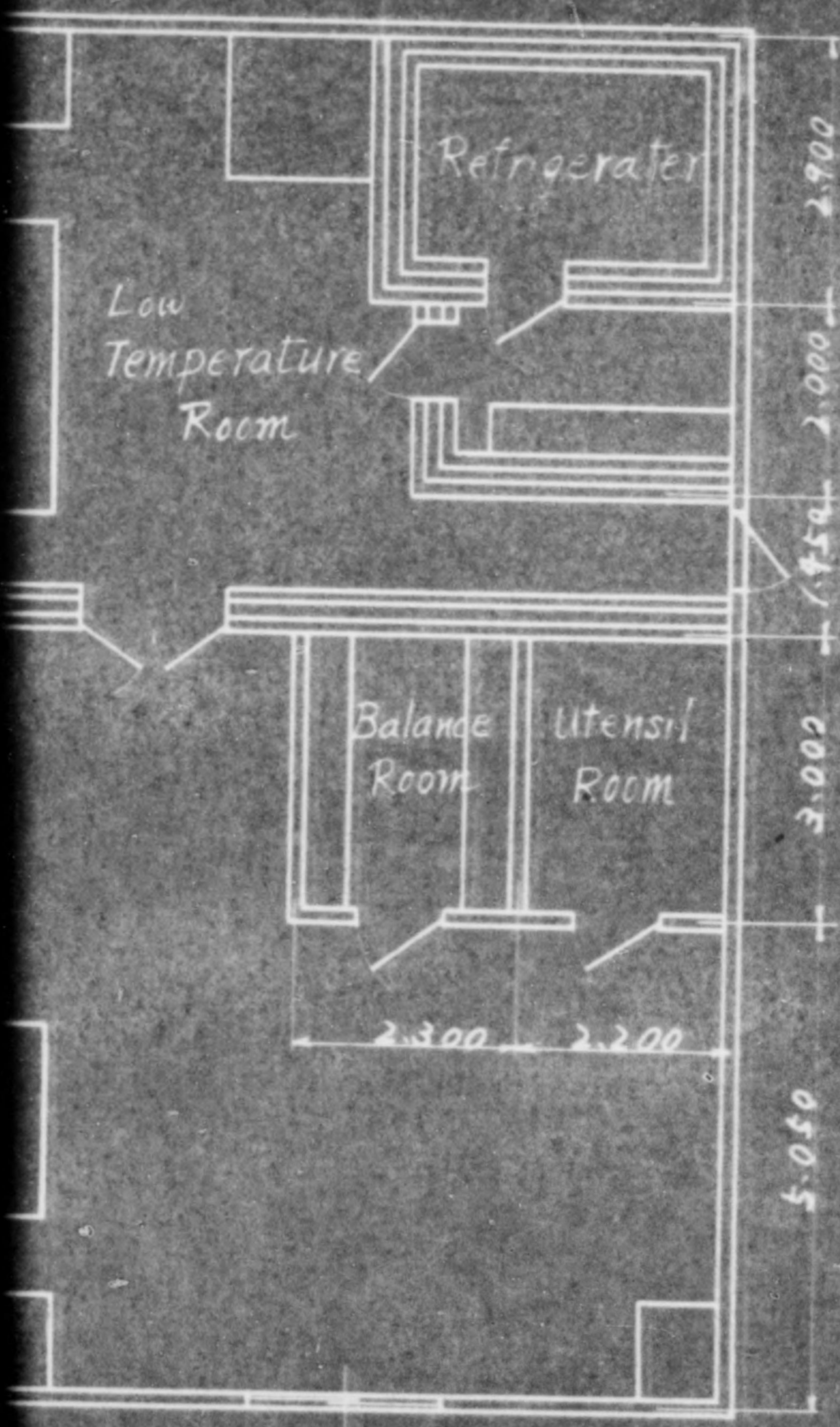
7 Refining Room 100

8 Culture Laboratory 100

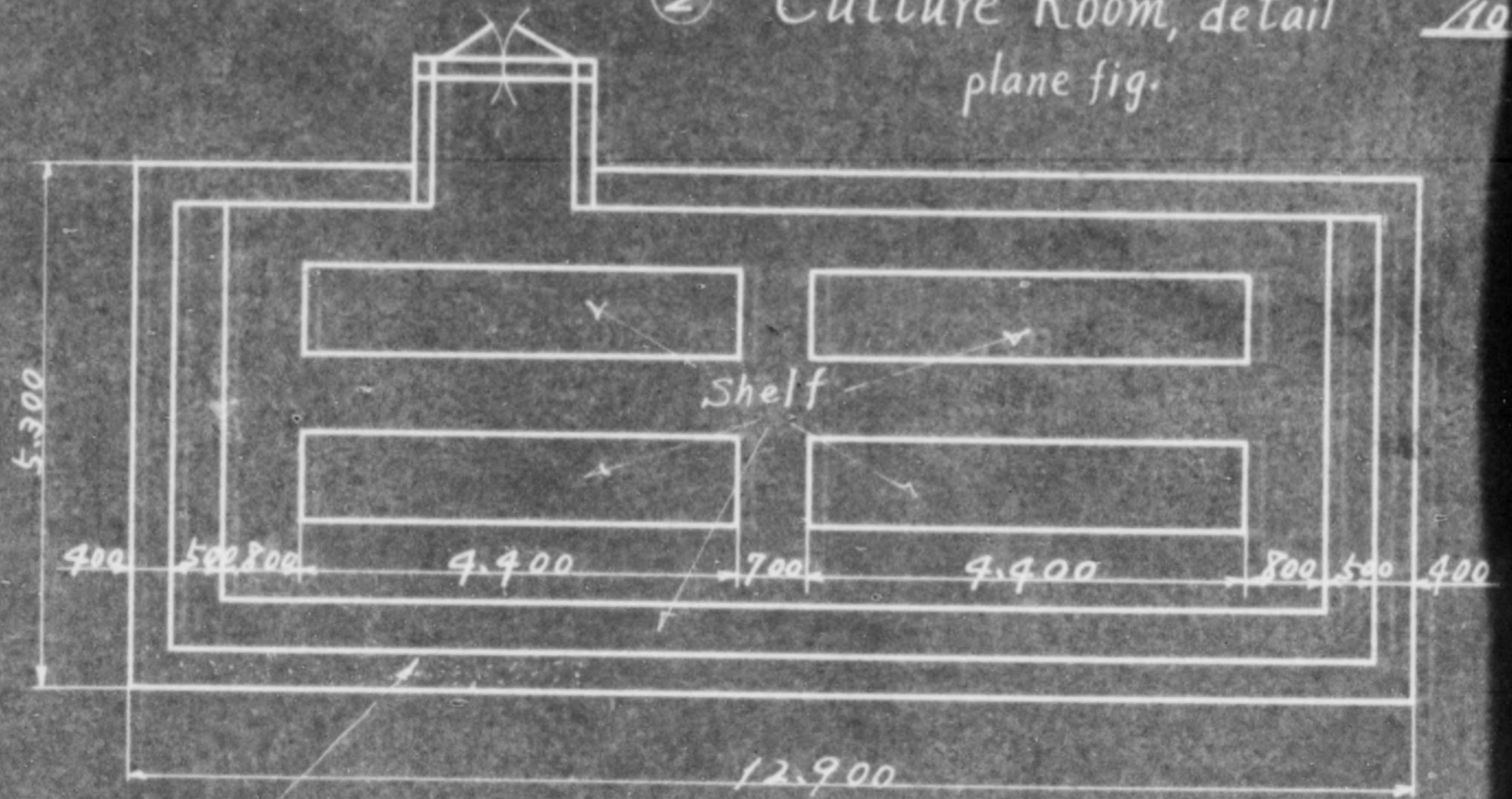
8.000

7.200

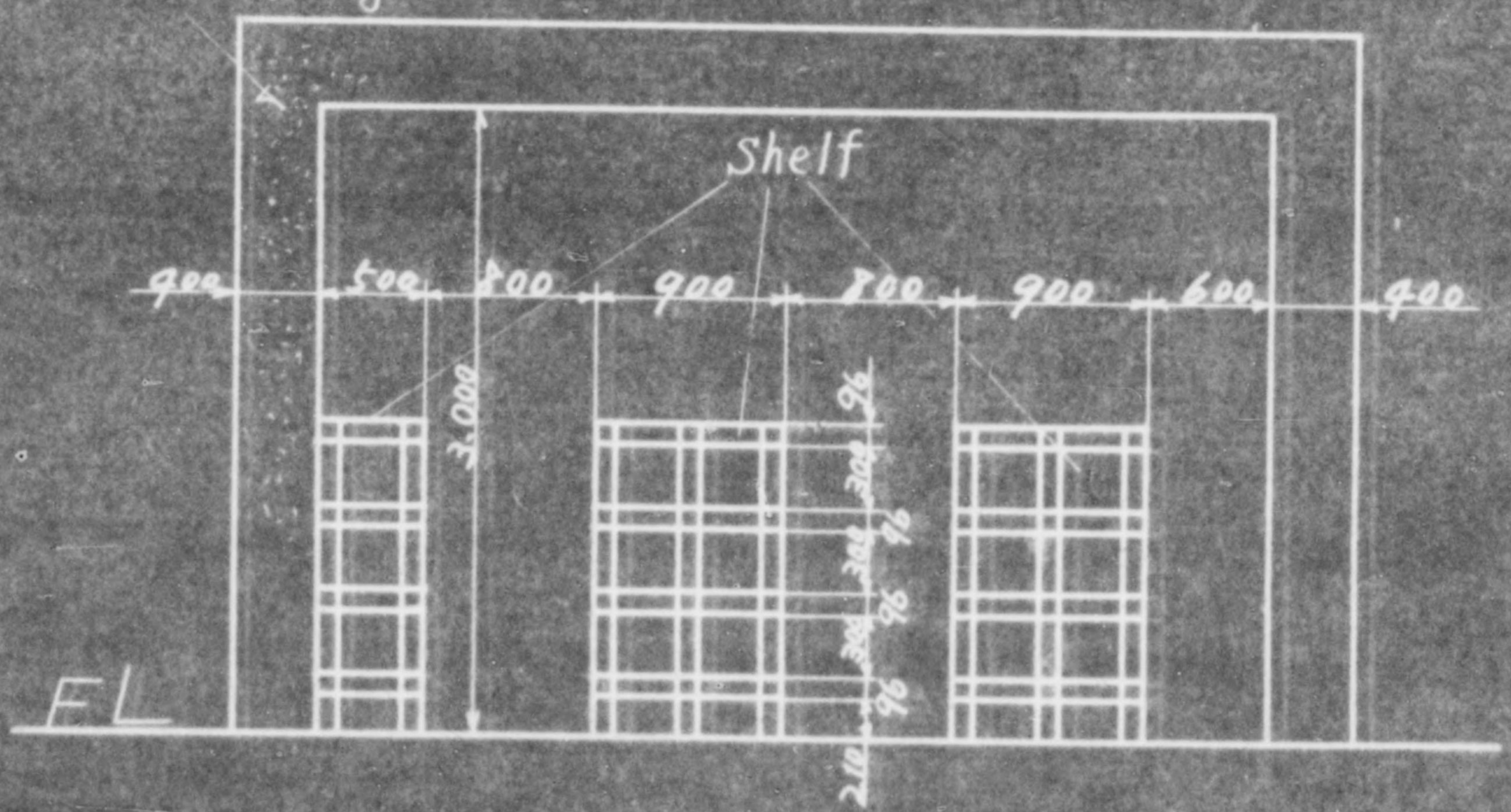
2.900



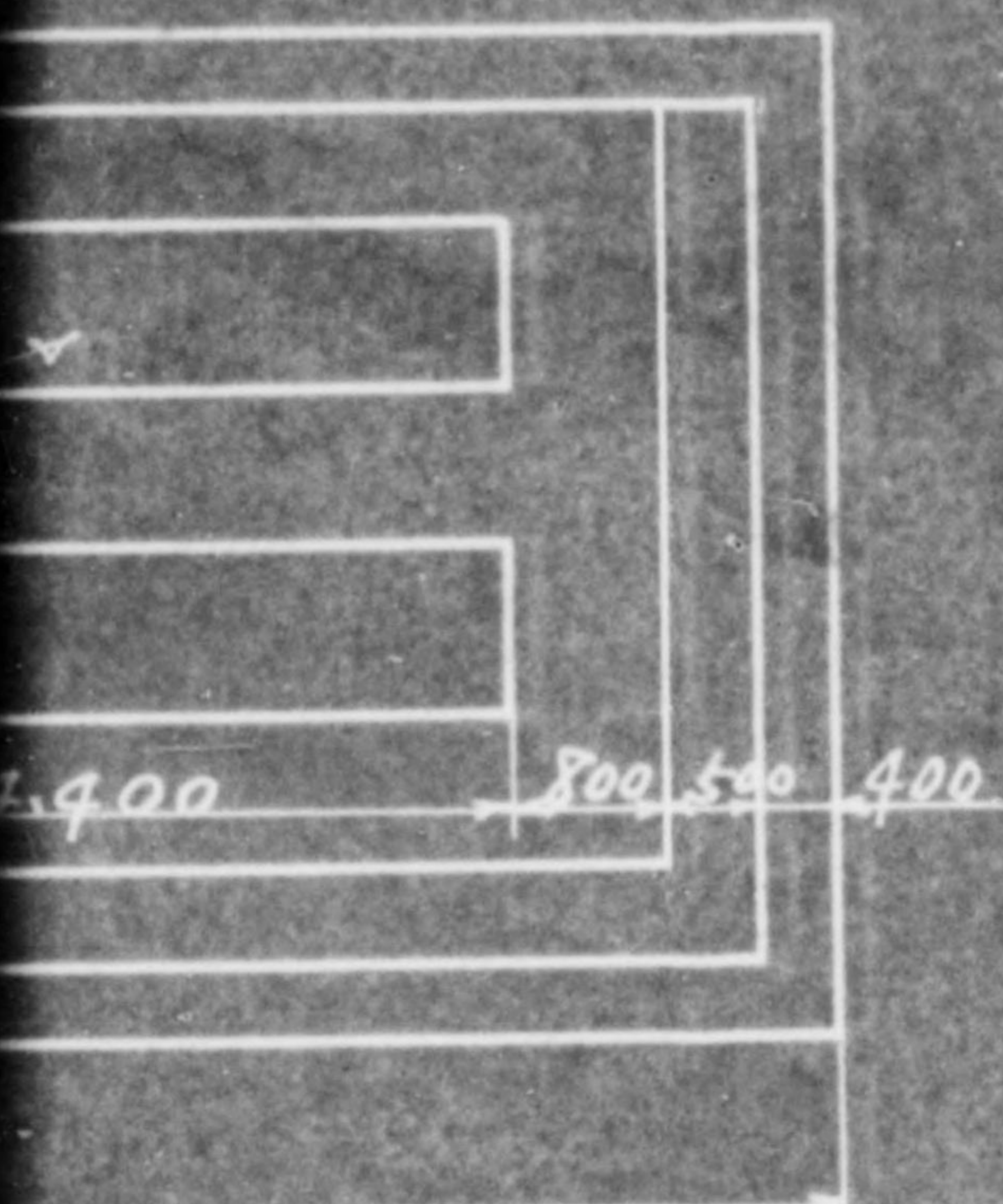
② Culture Room, detail $\frac{1}{100}$
plane fig.



Saw dust filling sectional fig. $\frac{1}{50}$



Room, detail $\frac{1}{100}$
pane fig.

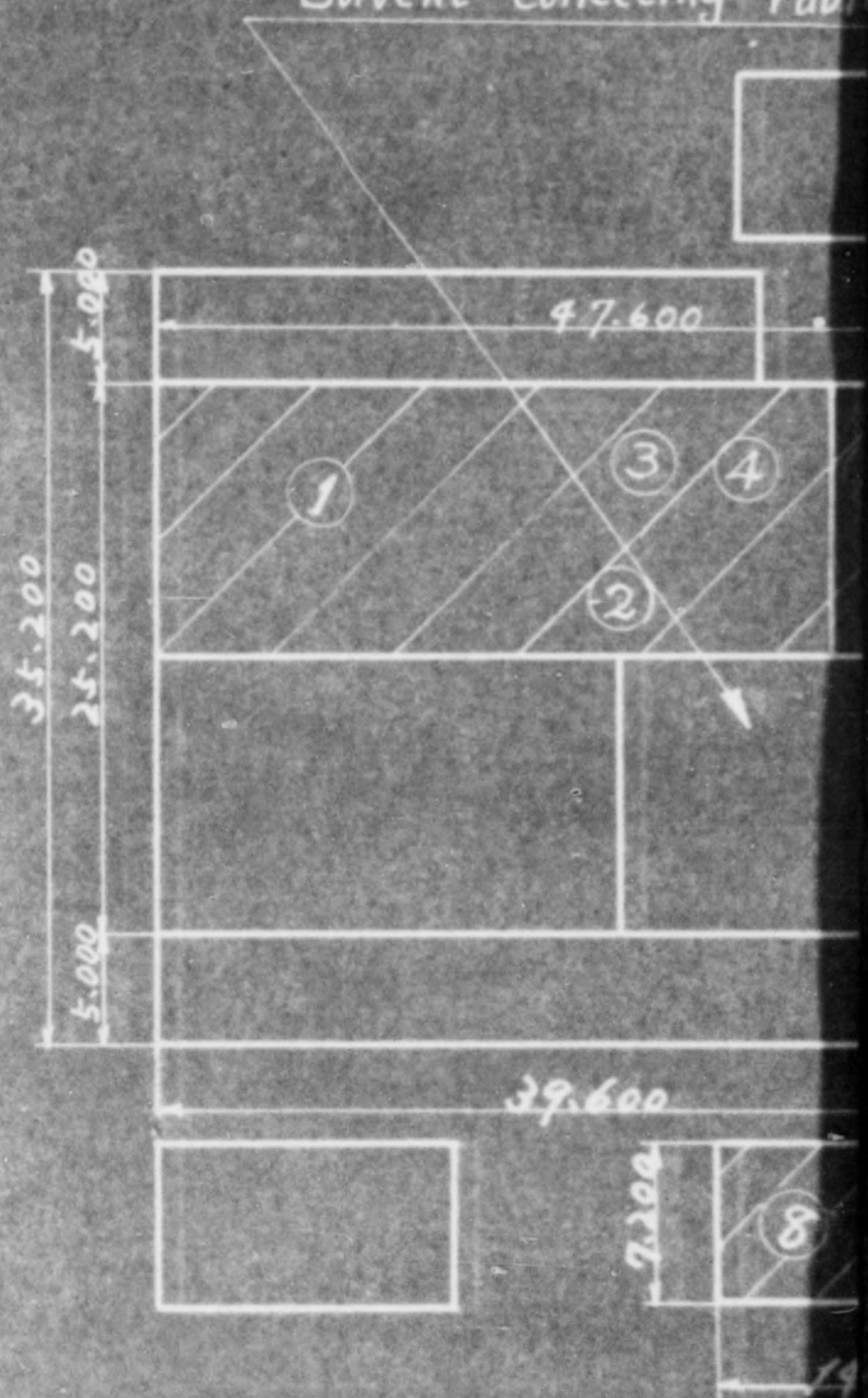


Sectional fig. $\frac{1}{50}$



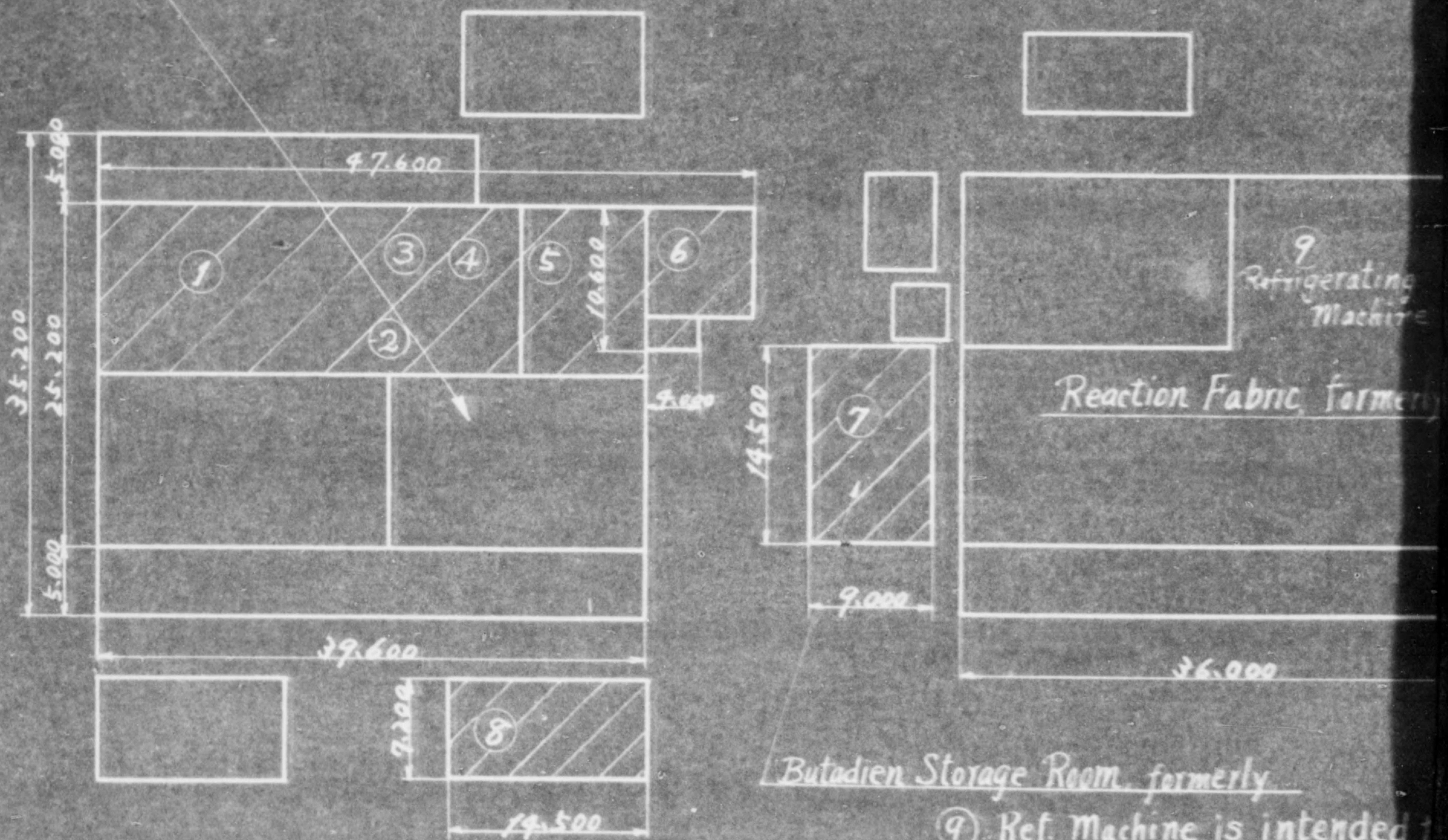
Position Diagram

Synthetic Rubber Factor
Solvent Collecting Fabr



Position Diagram

Synthetic Rubber Factory, at Miyosima,
Solvent Collecting Fabric, formerly

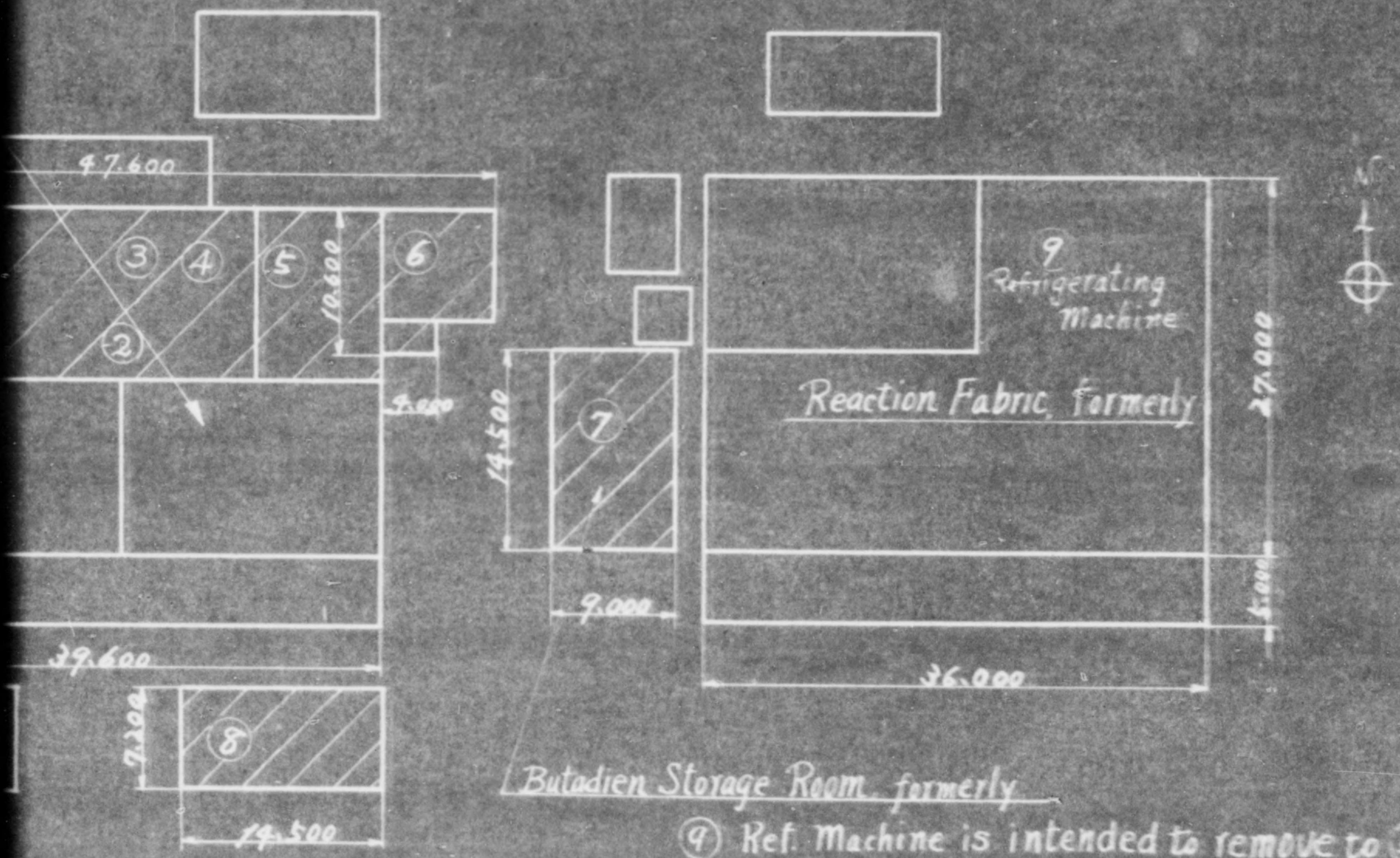


- ⑨ Ref. Machine is intended
- ▨ indicates the Part which is the Penicillin M

Diagram

Latex Rubber Factory, at Miyosima,
 Collecting Fabric, formerly

1/500

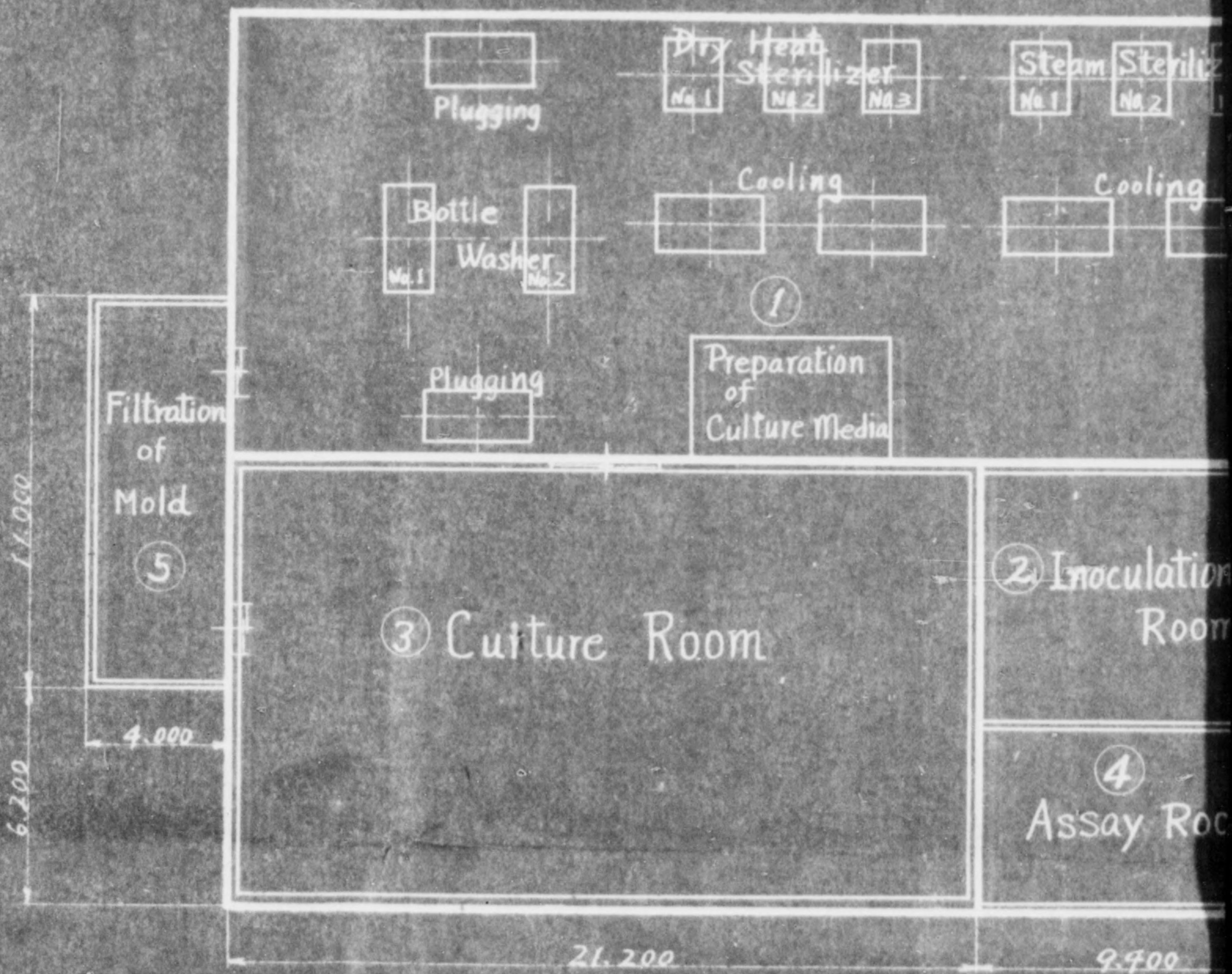


Butadien Storage Room, formerly

- ⑨ Ref. Machine is intended to remove to ⑤
- ▨ indicates the Part which is intended to use the Penicillin Manufacturing

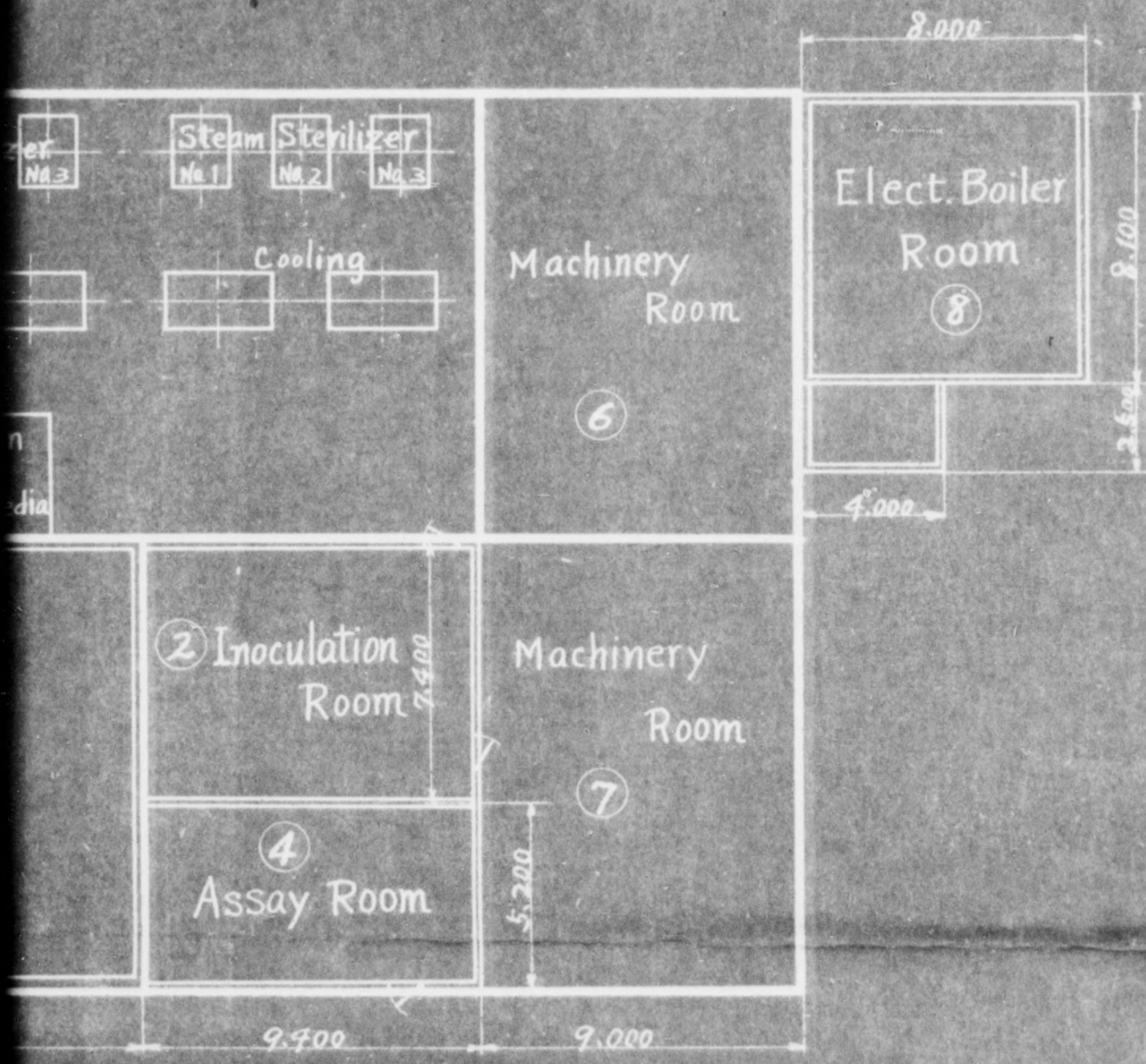
FIG. NO. 2

Plan of Penicillin Production
500^l/day Surface Culture



Penicillin Production

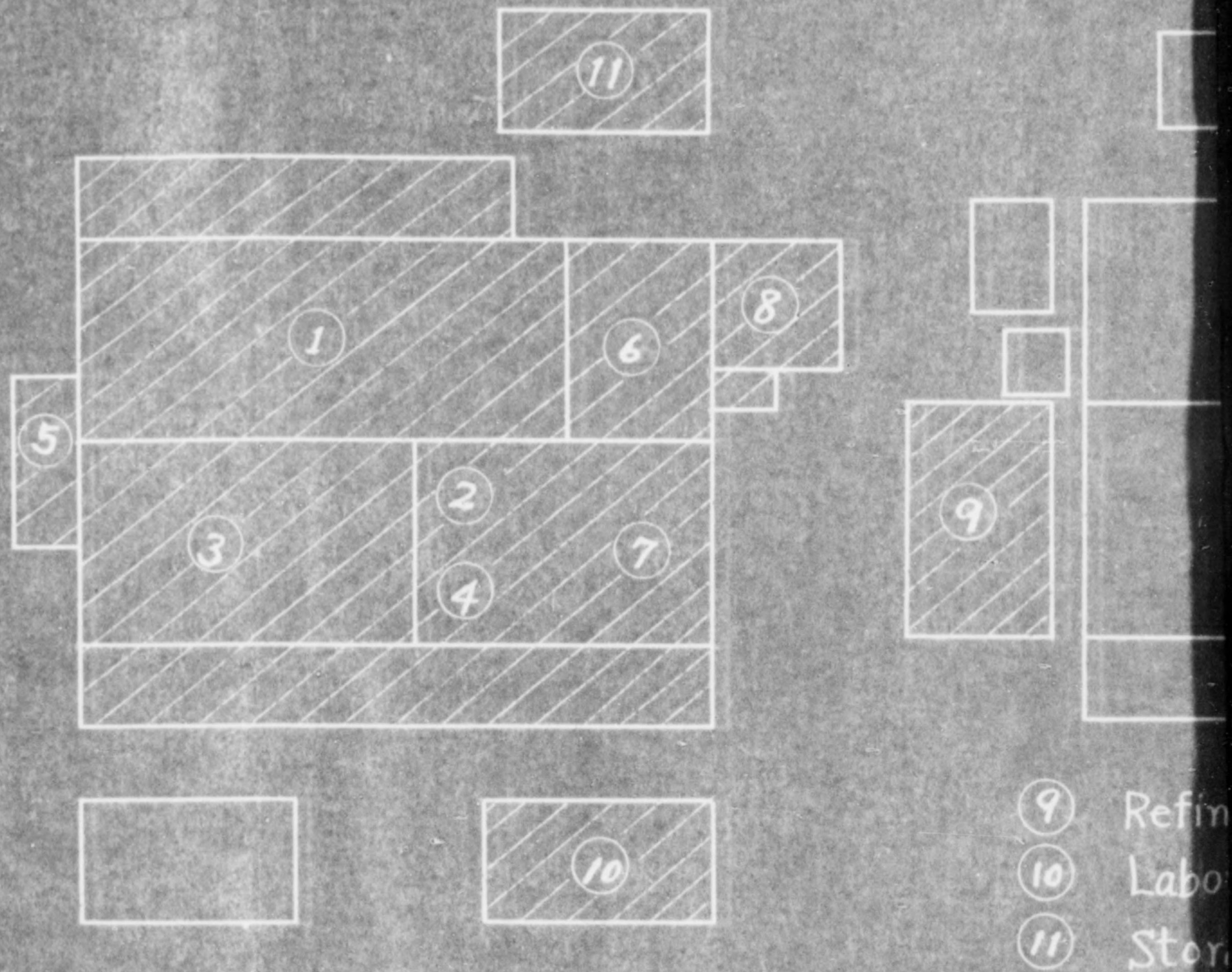
Day Surface Culture



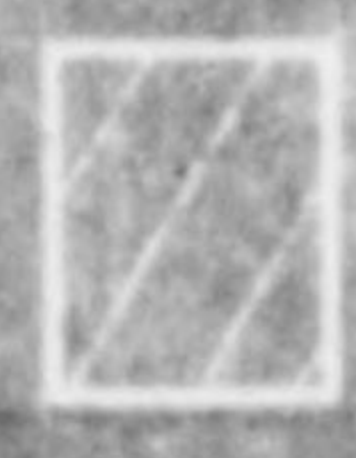
Bold Line indicates the Existing Structure

Position Diagram

The Whole View of Synthetic Rubber Factory, at Miyo

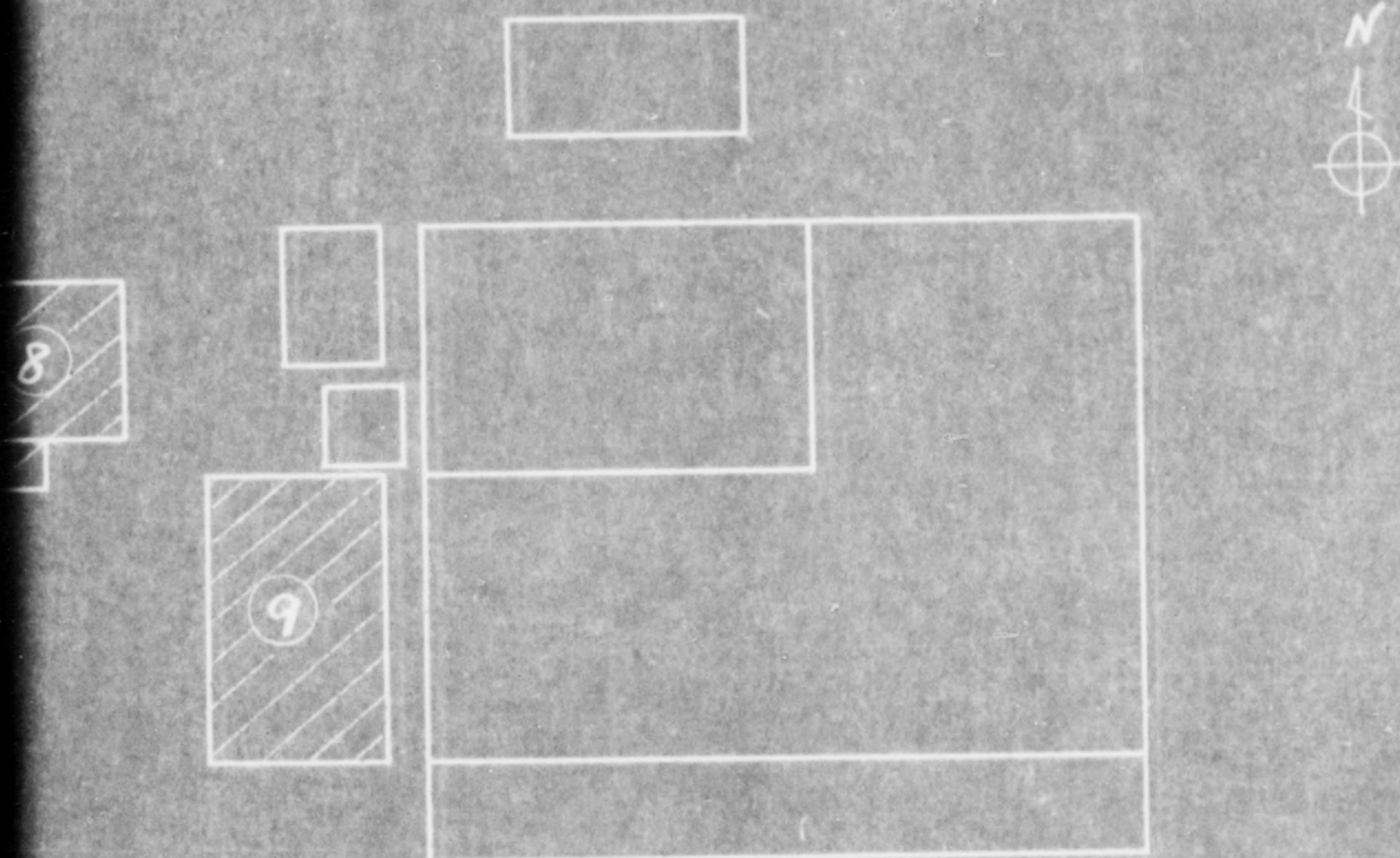


- ⑨ Refin
- ⑩ Labo
- ⑪ Stor

 indicates the Part which is intended to use the Penicillin Production.

cture

Rubber Factory, at Miyosima.

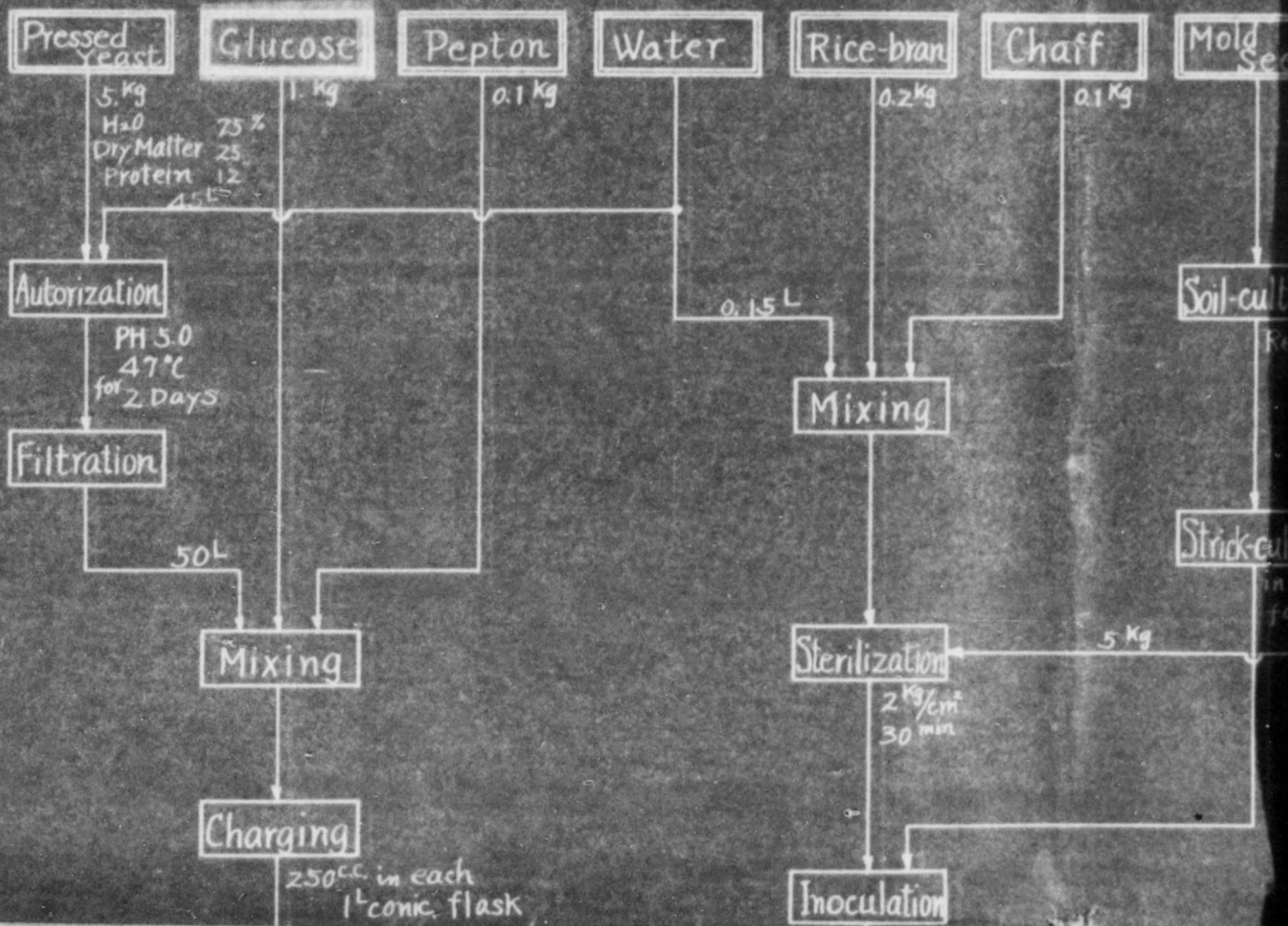


- ⑨ Refining Room
 - ⑩ Laboratory
 - ⑪ Storage Room of Raw Materials
- } is the same structure as that in the 50⁴/day culture

which is intended to use penicillin Production

Flow Sheet of Penicillin

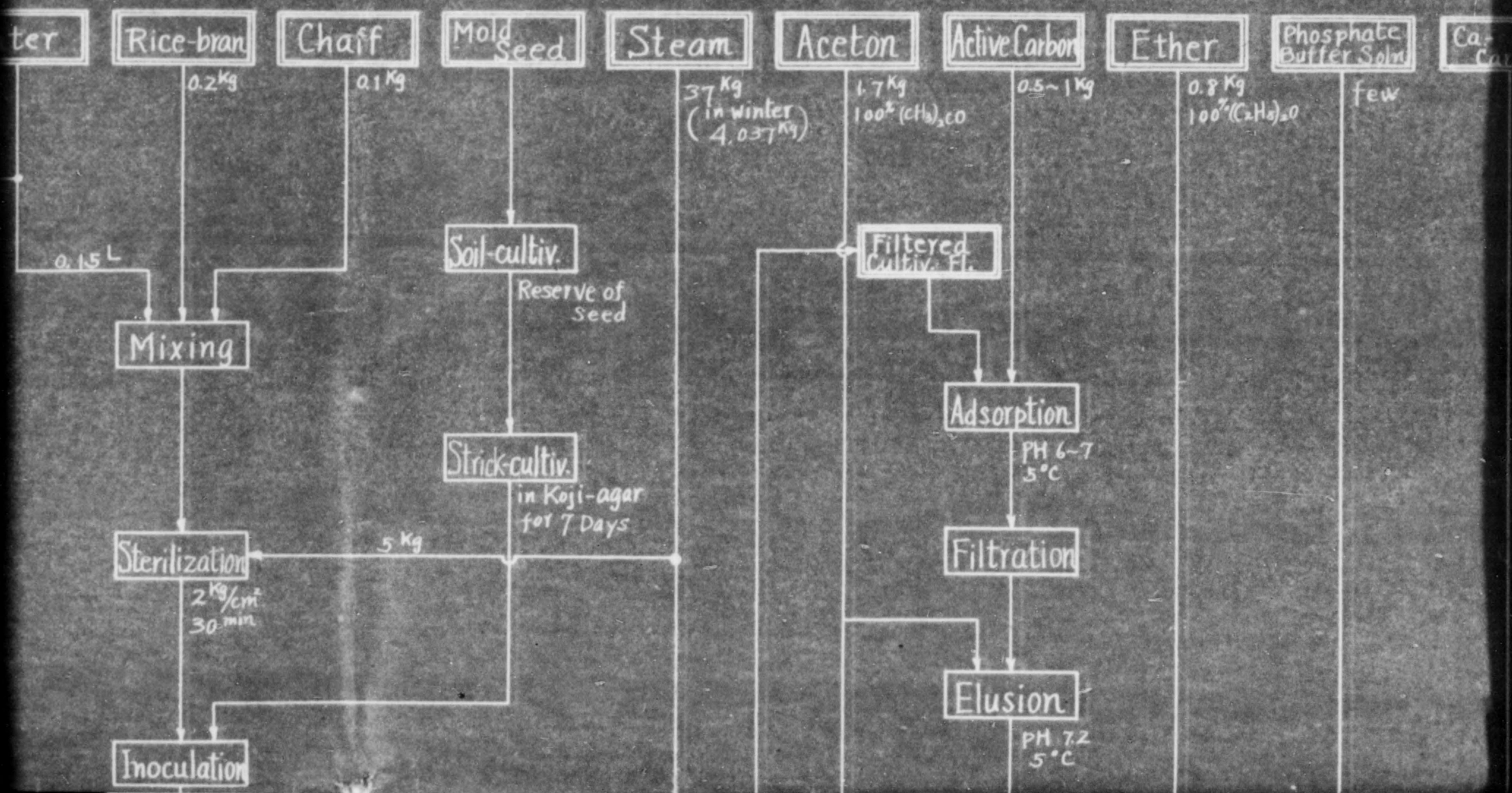
Surface Culture



Flow Sheet of Penicillin Production

50^L/day Cultivation

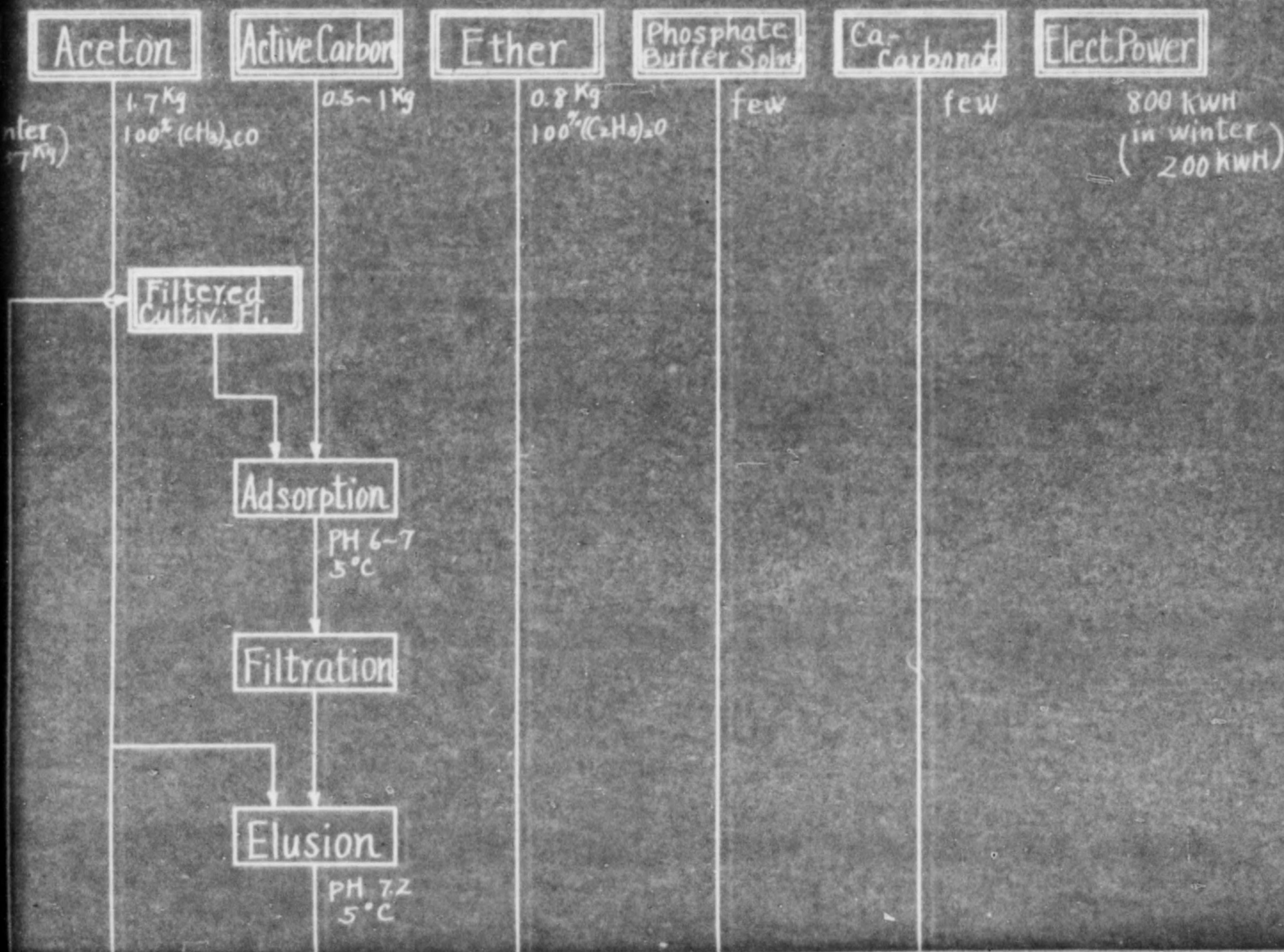
Surface Culture Method

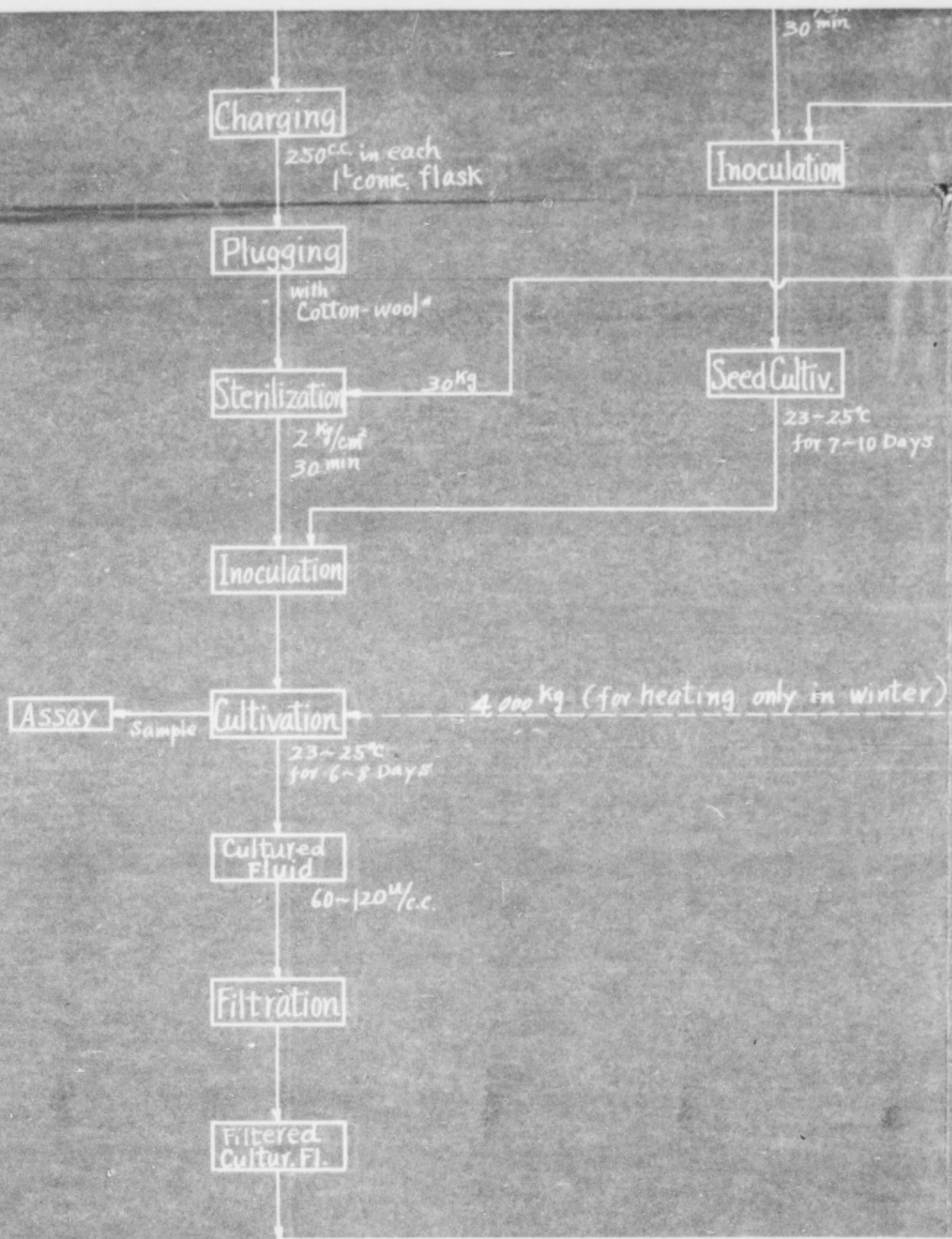


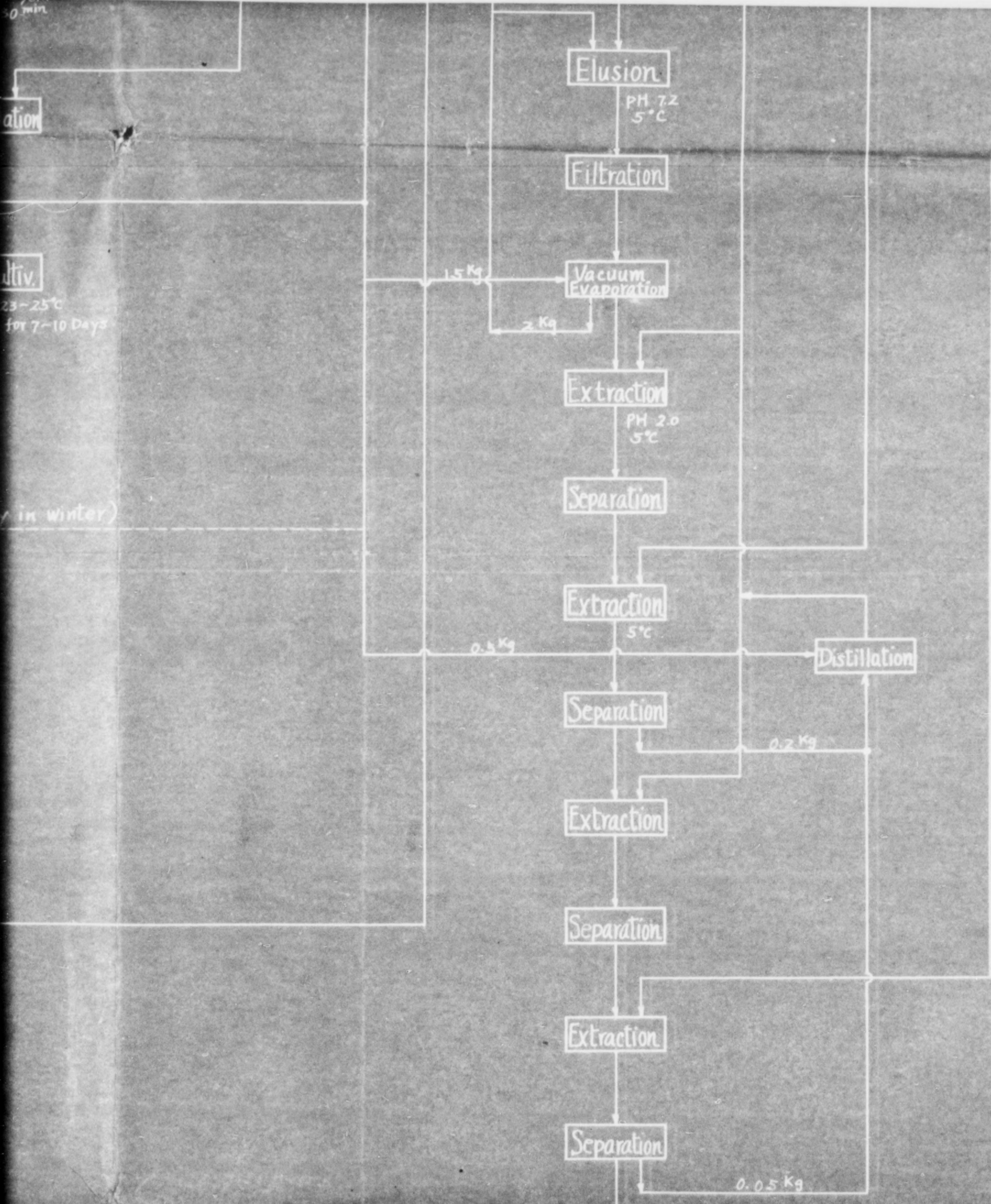
duction

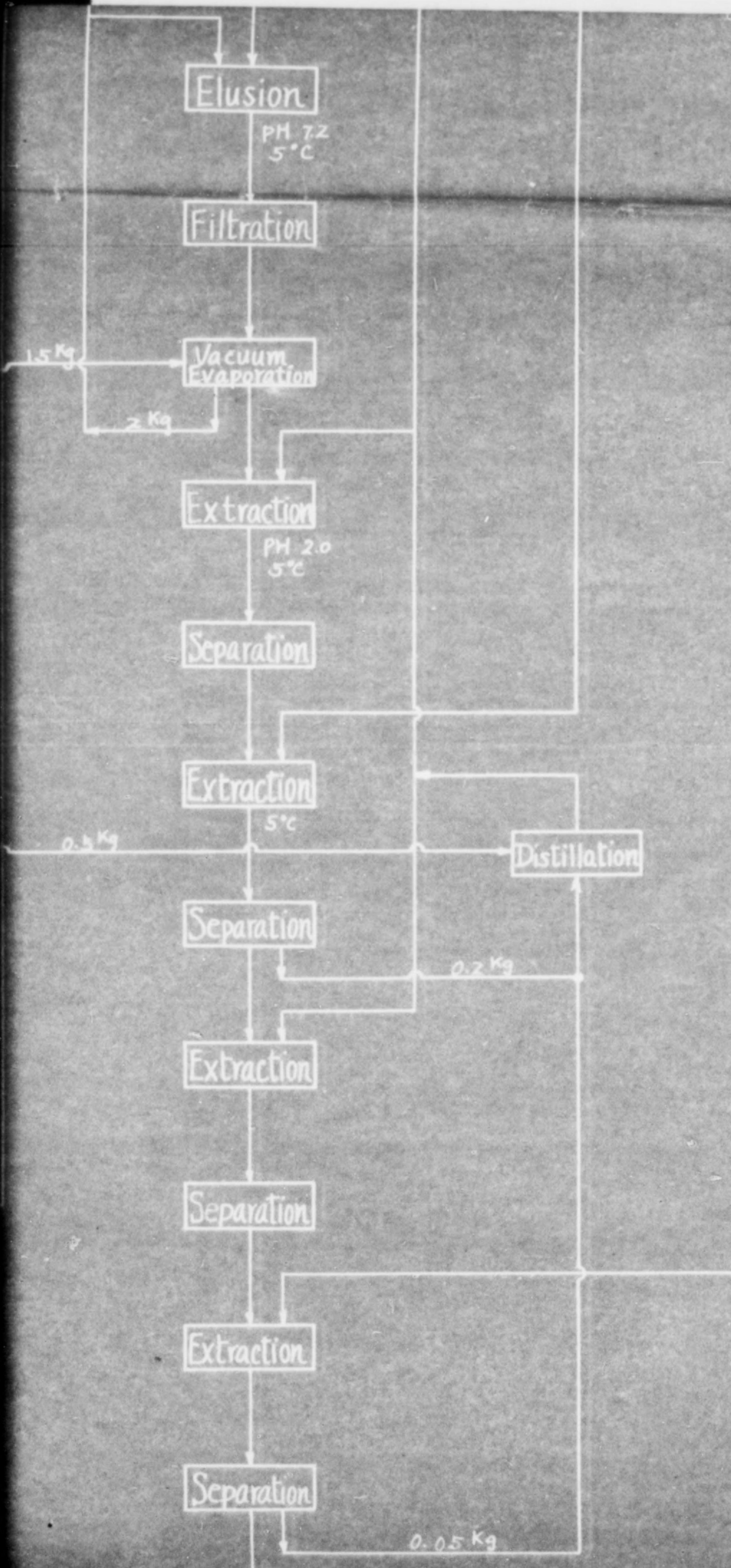
50^L/day Cultivation

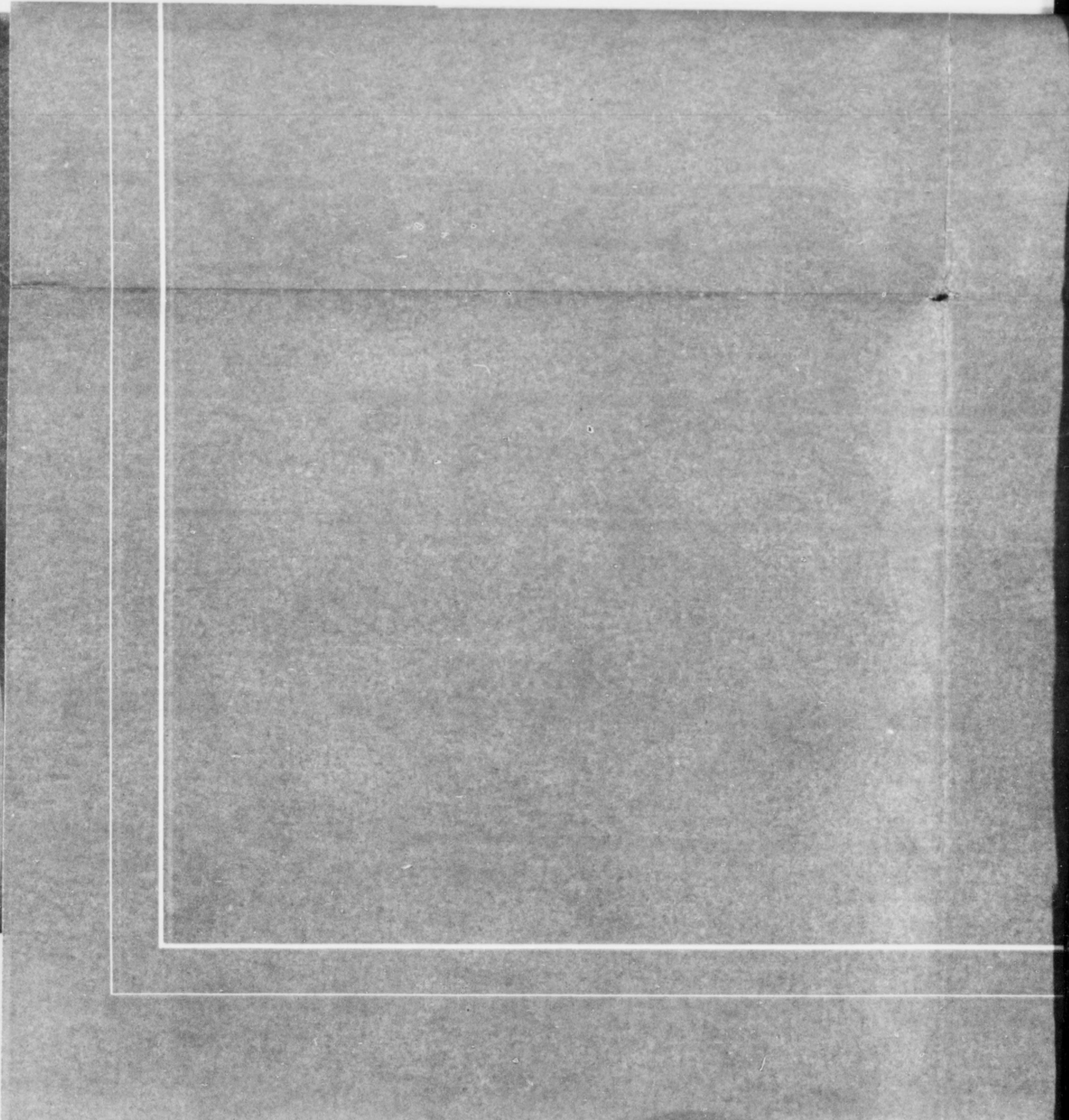
od

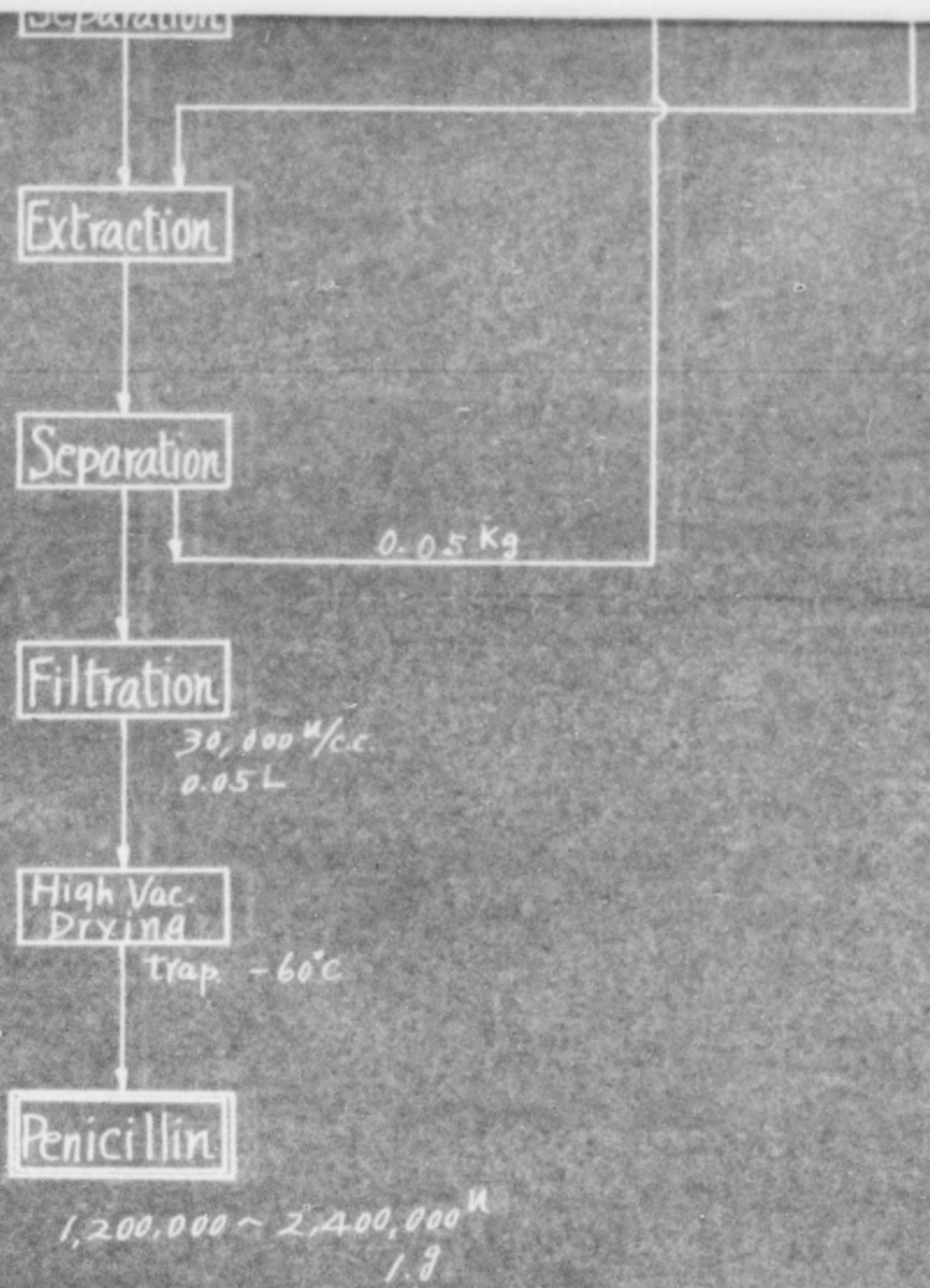












Separations

Extraction

Separation

Filtration

High Vac. Drying

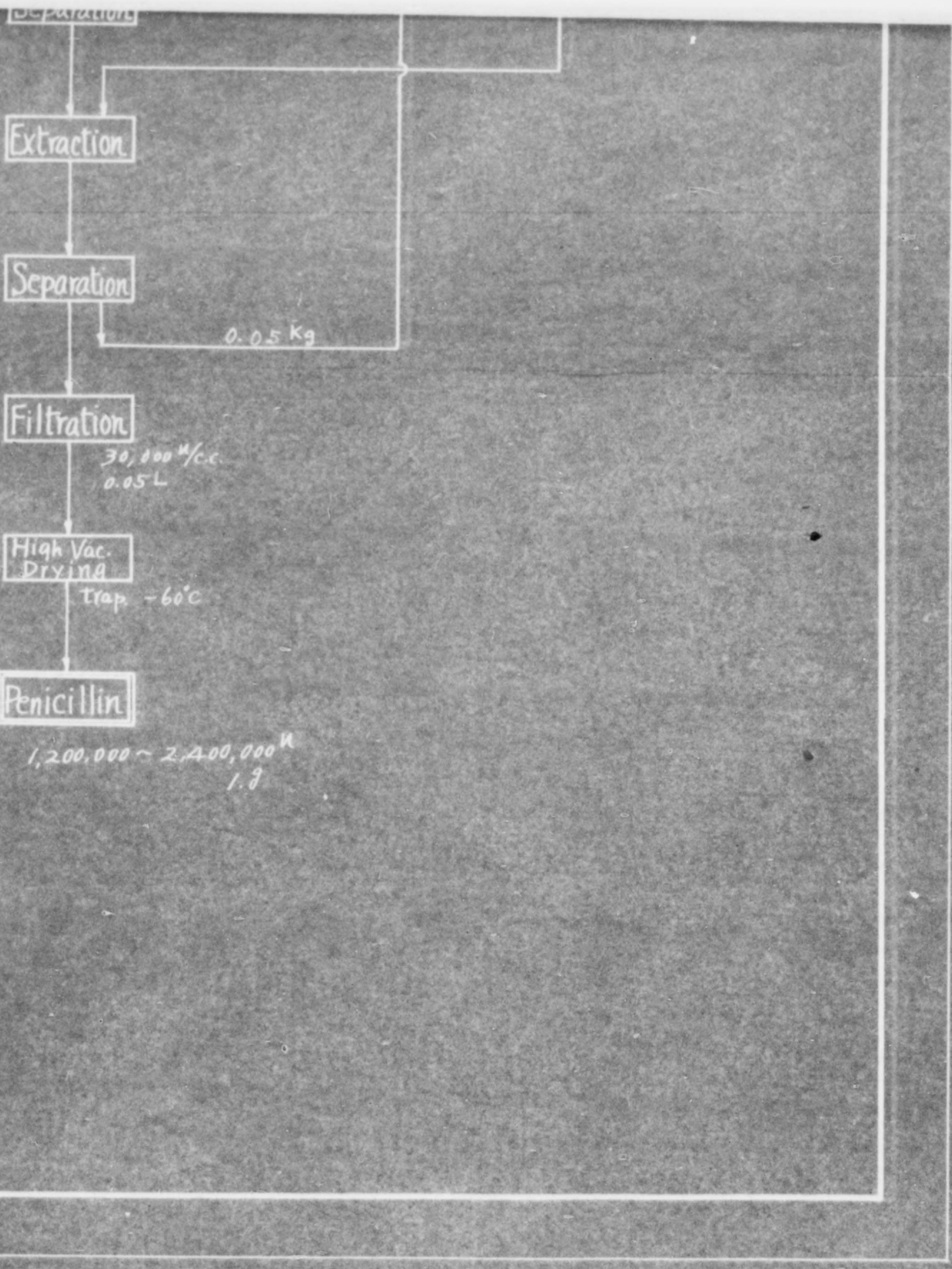
Penicillin

0.05 kg

30,000 μ /cc
0.05 L

Trap -60°C

1,200,000 ~ 2,400,000 μ
1.7



Requester No.	Name	Address	Dealer
21	Sakejiro Matsumoto	Mada machi Dunchou cho Dyo gun	Medical and Health Supply
22	Hisako Uwehara	Hojo cho Onsen gun	" " " "
23	Yoshio Sano	Uchiko machi Kita gun	" " " "
24	Yoshitaro Higaki	Ozu machi Kita gun	" " " "
25	Otschi Sawada	Huma machi Kamiubena gun	" " " "
26	Ichiro Tanaka	4 chome Shin machi Yahatahama	" " " "
27	Ishizaki Shoten	Marunouchi Uwajima cho city	" " " "
28	Yoshimatsu Den	Emura cho Uwajima city	" " " "
29	Shoichi Endo	Ote Dori Uwajima city	" " " "
30	Shizuka Joho	Uenomachi Uwa machi Higashi Uwa gun	" " " "

Supply

Registered Medical Supply Dealers

DECLASSIFIED E.O. 12065 SECTION 3-402/NNDG NO.

775013

Registration No.	Name	Address	Dealer
1	Setsubo Ochi	Doimura Uonagan	Medical and Health Supply
2	Ichiro Manabe	Mishima cho Uonagan	" " "
3	Mori mitau Miyasaki	" " " "	" " "
4	Kenbo Kuwabara	Higashimochi Saijo	" " "
5	Masayuki Aoki	No 936 Mihama City	" " "
7	Masao Kuwabara	Myugawa cho Shiro gun	" " "
8	Aritama Ioi	Mitsui Kurashiki Mikuba Imabari city	" " "
9	Yoshimichi Kato	Motomachi Imabari city	" " "
10	Terao Medical Co.	1 chome Joban cho Imabari city	" " "
11	Imabari Commercial Medical Corporation	Kita Shin machi Imabari city	" " "
12	Matsuyama Commercial Med Corporation	1 chome Sachi bana cho Matsuyama city	" " "
13	Shinichi Doi	Ichi ban cho Matsuyama city	" " "
14	Kobura Yakkan	4 chome Minatomachi Matsuyama city	" " "
15	Uchida Goshi Kaisha	1 chome Soyosaba cho Matsuyama city	Health supply
16	Koichiro Wada	No 30 Benten cho Matsuyama city	Medical and Health Supply
17	Kenko Murakami	No 2 of 11 Mishi hori bata cho Matsuyama city	" " " "
18	Matsumoto store	No 9 of 12 Gembayama cho Matsuyama city	" " " "
19	Ehime Yakuhin Shoji Kabushiki Kaisha	Madamachi, Dancho cho Iyo gun	" " " "
20	Doi Shoten	" " " "	" " " "

Supply Method Used For Calculation of Points

- A Clinics with ^{chief} specialized doctor for each doctor 10 pts.
- A' Clinics with hired doctor for each doctor 7 pts.
- B Hospital and clinics with ^{chief} specialized ~~doctors~~ ^{druggist} for each druggist 5 pts.
- C with hired druggist, nurses and helper for each 2 pts.
- D Number of bed for each bed .2 pts.
- E Coefficient for various specialist (average number for General Hospital)
- F Out patient (including patients ~~whom~~ ^{whom} the ~~visit~~ doctor visits)

$$(A + A' + B + C + D) \times E \times F = \text{points given}$$

F = average patient per day (out patients and the patients whom the doctor visit)
 Until 10 patients, 0.1 will be added for increase in patients from 1 to 10
 Fraction will be ~~carried to next decimal~~ ^{carried to next whole}

To Chevre M. S. Beaman

From Mayor of Newayama

Regarding the Chlorination of Water

Thank you very much coming the other day a

5,249,008 1947

2,371,270

1,881,840

500
10
500

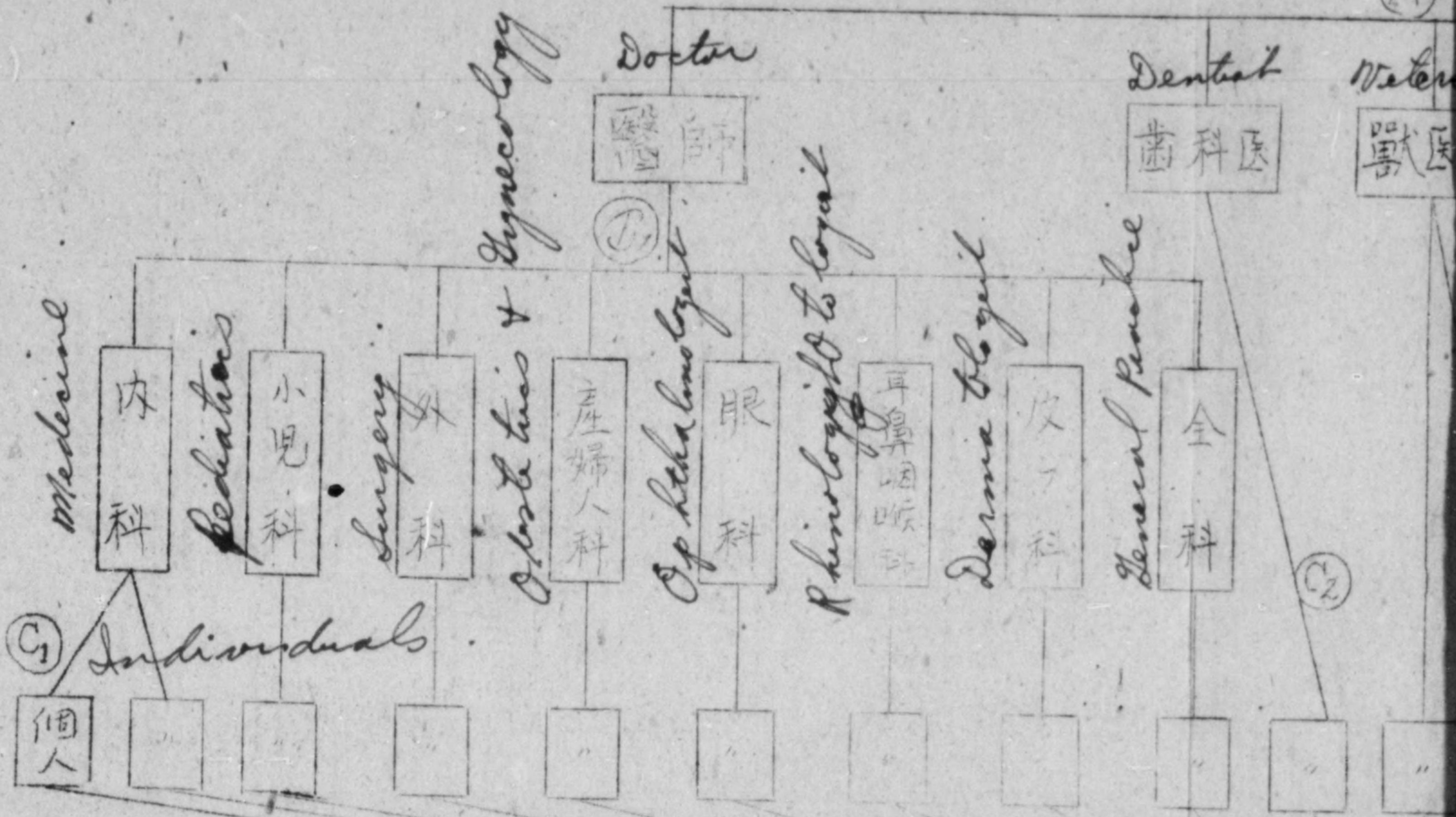
1.4 -

500 | 10.00
1000

2%

Supply

厚生
Prep
縣



Method of deciding the ratio

(割当決定法)

- According to efficiency, amount required and amount received

① 各業態別需要量並に収入額に依る 地方販賣
- According to the coefficient of class of specialist

② 専門別係数に依る Local ↑
- According to the condition of business

③ 各業者の営業状況に依る 中央販賣
- According as to need from business classification

④ 業務別需要に依る Central ↓

Welfare Minister

厚生大臣

Prefectural Governor

縣知事

(副當)

(A)

Dentist

齒科医

Veterinarian

獸医師

Druggist

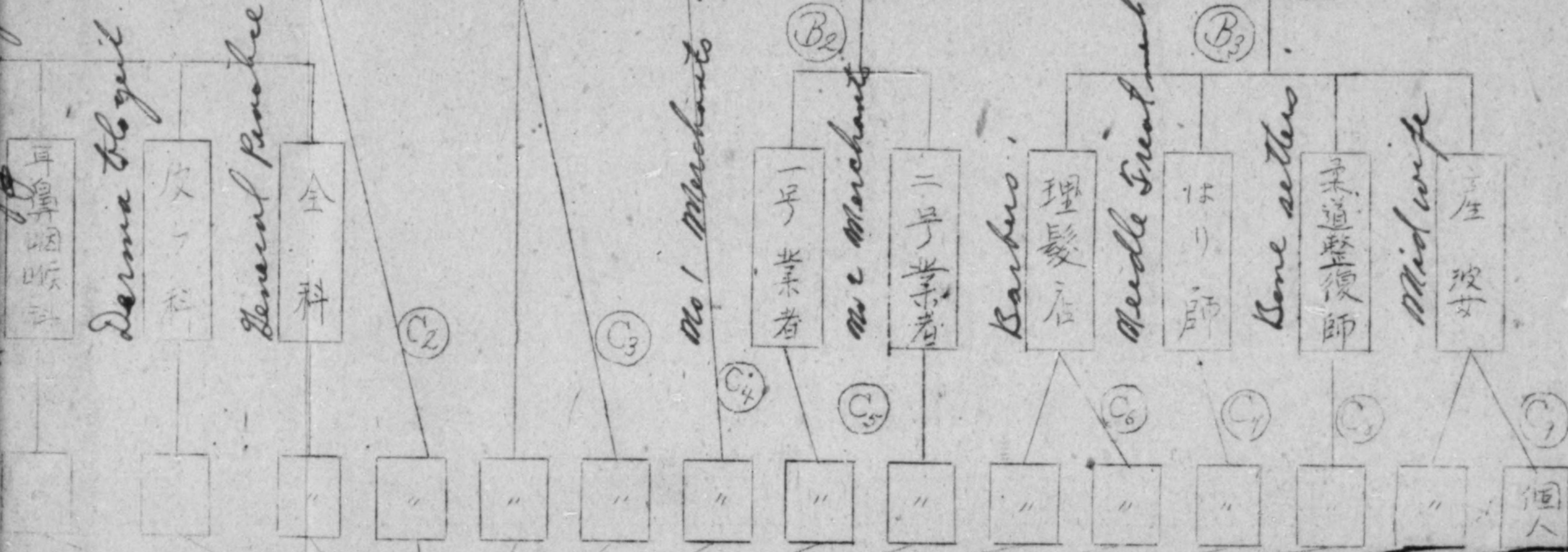
調劑

Retail store

小賣

Others

其他



the nature

amount required and amount received
percent of
nature of specialist
condition of
business
from
business classification

地方販賣業者

Local Merchants

中央販賣業者

Central Merchants

Follows the formula for deciding prices.

- (C1) 各診療所別算定式に依る
- (C2) " " " " " "
- (C3) " " " " " "
- (C4) " " " " " "

regarding whether or not the
 Mishin Chemical Company carried
 out any blackmarket deal.

Regarding the investigation ask by you
 whether the Mishin Chemical Company
 carried out any blackmarket deal,
 we believe none has been carried out.

1. Regarding whether the penicillin has been
 manufactured ~~to~~ aside from the report
 of the company.

(a) From the books of the company regarding
 labors it has been found that there
 washers for the penicillin plant has
 increased as the research progressed. As
 in the separate sheet, the ~~the~~ men increased
 as the ~~production~~ facilities of production
 increase accordingly as reported by the
 Company. We believe therefore that
 the Company did not produce as much
 penicillin before October.

(b) ~~The books~~ when the book which has
 the list of material ordered from Orskan
 was checked over ^{with} other books it was
 found to check. ~~From~~ By checking the
 material used for the production of
 penicillin we believe that aside
 from the product reported by the Co.
 no other has been produced.

(c) The fact that the Company has reported
 low production of penicillin until
 recently was due because they have
 been using B₂ type, which had
 caused low concentration ^{and} difficulty in
 purification.

From 9 Dec. They have been using Q172 which was received from SCAI, although the Company bought efficient vacuum pump. Because of the lack of parts it has not been working well until Nov. Also regarding the permit for changing the use of refrigerating plant from DHG, the permit was not received promptly. We believe such process of making dry ice from liquid CO₂ has slowed down production. Therefore we cannot believe that the company has been reporting low production to sell the rest thru black market.

- (1) Aside from the small amount used for experimental purpose, checking over the amount in stock we cannot believe the penicillin has passed out thru illegal channels.
- (2) As according to the copy of the material received from Orsaka, the bottle although was received on 27 Aug. the rubber stopper and cap was received on 22 Oct. The machine for putting the cap on the bottle was received on 7 Nov. In other words it was after Dr. Hamilton's visit that they were able to bottle the penicillin. Before that the company had no container. The ^{labels for} labels and wrapping paper are at present being sent to Orsaka. We therefore believe that in the past the company did not sell any penicillin as a private stock.
- (3) We have investigated the doctors, hospitals and druggists of the New but found no trace of blackmarket penicillin from the Co.

- 12 Roberin styloschloide
- 13 ~ ~ ~ for injection
- 14 Hydrogen peroxide
- 15 dilute alcohol.
- 16 Quinine injection
- 17 Quinine vial ampule.
- 18 ethyl chloride.
- 19 silver colloide.
- 20 Bismuth subsalicylate
- 21 Bismuth subsalicylate for injection.
- 22 Mercuric chloride for disinfection.
- 23 Kefnol iodine
- 24 Sodium chloride solution.
- 25 Thiantal.
- 26 Sodium bicarbonate tablets
- 27 Thioferol.
- 28 Sulfaguanidine
- 29 Sulfaguanidine tablets.
- 30 Sulfamine tablets
- 31 Powder of digitalis
- 32 Powder of digitalis for injection
- 33 Powder of Japanese chestnut
- 34 Potassium bromide.
- 35 Protein silver
- 36 Scopolamine hydrobromide
- 37 Maphazol.
- 38 Ether for anaesthesia
- 39 Chloroform
- 40 Iodine
- 41 Extract of scopolia

In order to ease up the circulating fund difficulties now experienced by the manufacturers, Central dealers, local and retail dealers, transactions will be made drafts. It will be made so that this will be accepted by the banks - (transaction for rationed drugs)

Medical Supply

Dental gold will be one of the 13 items designated in the Official Government Bulletin as far as

the noble metals designated are

Gold (5 grams pure gold) platinum (0.5 gram metal) silver (25 gram metal) platinum foil. platinum gold non casting silver alloy casting silver alloy. pure silver (packing) silver alloy (packing) nickel-chrome alloy, heat metal solder metal, silver-tin alloy.

Users.

Dentist, Hospital with dental clinic and dental schools.

Dealers.

Those who has been registered in the Ken Ken will determine the dealers, taking into consideration, the capital, financial condition whether or not they have a place for safe keeping.

The Ken has not yet received official notification from the Welfare Ministry (Mr. Fujita believe this due to the strike now being carried out by the communication and transportation workers.)

Drugs which went off the ration

- | | |
|----------------------------------|--|
| 1 zinc oxide ointment | 9 solution of eprenamine hydrochloride |
| 2 aspirant. | |
| 3 acetosulfamine injection | 10 Procain hydrochloride for injection |
| 4 aminopyrine tablets | |
| 5 aminocordin | 11 Procain hydrochloride tablets |
| 6 insulin | |
| 7 Calcium chloride | |
| 8 Calcium chloride for injection | (over) |

List of allotment of medicine

Item	Classification Quantity	Physician	Dentist	V
Zinc oxide		50,000 ^{Kg}		
Zinc oxide ointment		50,000		
Rivanol		1.800 ^K		
Acetylsalicylic acid		195,000		
Acetylsalicylic acid tablets			11,400 ^T	
Aminopyrine		70,000 ^K		
Aminopyrine tablets		20,000		
Alcohol		300,000 ^K	40,000 ^K	
Caffeine with sodium benzoate		7,000 ^K		
Calcium chloride		100,000 ^K		
Calcium chloride for injection		35,570 ^A		
Solution of epinephrine hydrochloride		10,000	3,300	
Ephedrine hydrochloride		400g		
Procaine hydrochloride		1,000 ^{Kg}	200g	
Procaine hydrochloride for injection		227,000 ^A	13,000	
Labeline hydrochloride for injection		750 ^A		
Solution of hydrogen peroxide		198,000 ^{Kg}	39,000	
Aromatic castor oil		118,500 ^{Kg}		
Mild tincture of iodine		41,000 ^{Kg}		

Statement of medicine for the month of Feb. ^{and} Mar. 1948. (No. 1)

Location City	Physician	Dentist	Veterinarian	Compounding of medicine	Retail of medicine	Other	Remain- der	Total
	Kg 50,000						2,500	Kg 52,500
	50,000						2,000	Kg 52,000
	K 1,800						0	K 1,800
	195,000			12,000			0.850	K 207,850
		11,400 ^T			17,100		0	28500 ^T
	K 70,000						2,600 ^g	K 72,600
	20,000				16,000		0	36,000 ^T
	300 ^K 000	40 ^K 000	20,000	20,000			28,000	Kg 408,000
	K 7,000			800 ^g			0	K 7,800
	K 100,000						1,500	Kg 101,500
an	35,570 ^A						0	35,570 ^A
Hydrochloride	10,000	3,300					40	13,340
	400 ^g						75 ^g	475 ^g
	Kg 1,000	200 ^g					0	Kg 1,200
tion	227,00 ^A	13,000					0	240,00 ^A
ction	750 ^A						0	750 ^A
	Kg 198,000	39,000			160,000		0	Kg 397,000
	Kg 116,500			7,500	32,000		0	Kg 156,000
	Kg 46,000		10,000		60,000		0	Kg 116,000

Item	Classification -	Physician Quantity	Dentist
Tincture of cinchona		Kg 80,000	
Indramin		200g	
Quinine hydrochloride		Kg 96,000	
Quinine hydrochloride tablets		10,750T.	
Quinine injection		39,700A	
Bagnon injection		19,100A	
Hydroquinine		Kg 861,000	
Quinine sulfate tablets		416,780T	
Compound tincture of gentian		Kg 251,000	
Glycerin		Kg 557,000	18,000
Solution of cresol soap		Kg 100,000	70,000
Sesame oil		Kg 12,000	
Colloidal silver		Kg 2,000	
Solution of potassium acetate		Kg 7,000	
Sodium salicylate		Kg 52,000	
Santonin tablets		64,700T	
Bismuth subsalicylate		Kg 28,000	
Sodium bicarbonate		Kg 100,000	Kg 500,000
Silver nitrate		Kg 2,000	
Alcohol for disinfection		200,000	

No. 2

Application -	Physician	Dentist	Veterinarian	Compounds mg of medicines	Retail of m.	Other	Remain	Total
Quantity								
	Kg 80,000						0	Kg 80,000
	200g						0	200g
	Kg 96,000						0	Kg 96,000
	10,750T.				10,750		0	21,500T.
	59,700A						0	59,700A
	19,100A						0	19,100A
	Kg 861,000			45,000				Kg 906,000
	416,780T						0	416,780T
	Kg 251,000		7,000	22,000			0	Kg 285,000
	Kg 557,000	18,000		12,000			0	Kg 587,000
	Kg 100,000	70,000	15,000		300,000		83	Kg 1468,000
	Kg 12,000						500g	Kg 12,500
	Kg 2,000						0	Kg 2,000
	Kg 7,000						500g	Kg 7,500
	Kg 52,000						500g	Kg 52,500
	64,700T						0	64,700T
	Kg 28,000						150g	Kg 28,150
	Kg 100,000	Kg 500,000	70,000	20,000			0	Kg 1530,000
	Kg 2,000						0	Kg 2,000
	200,900				Kg 40,000	40,000	2,000	Kg 282,000

Item	Classification	Physician	Dentist
		Quantity	
Purified iodine		kg 3,400	
physiological solution of sodium chloride		53,000	
Tar and sulfur paste		kg 100,000	
Albumin tannate		100,000	
Mitigal		191,000	
Bismuth subsalicylate for injection		17,500A	
Theophylline with sodium acetate		1,400	
Sulfaguanidine tablets		2,600	
Sulfapyrimidine		kg 390,000	
Sulfapyrimidine tablets		3,230T	
Sulfathiazol		kg 50,000	
Sulfapyridine injection		2,180A	
Sulfanilamide tablets			2,720T
Digitalis injection		cc 18,000	
Sevoctia		kg 90,000	
Nupercain		500g	100
Ergot		kg 6,000	
Barbital		kg 2,000	
Ethyl chloride		kg 10,000	
Mercuric bichloride for disinfection		700g	
Sulfamethoxythiazol tablets		33,400T	

No. 3

Application	Physician	Dentist	Veterinarian	Compounding of M.	Retail of M.	Other	Remainder	Total
Quantity								
	Kg 3,000			3,000			Kg 1,300	Kg 7,300
oxide	53,000						0	53,000
	Kg 100,000				115,000 7,000		0 500g	215,000 191,500
	100,000				91,000		500g	Kg 191,500
	191,000			4,400	30,000		0	Kg 225,400
ion	17,500A						0	17,500A
te	1,400						0	Kg 1,400
	2,100				2,100		0	5,200T
	Kg 390,000						0	Kg 390,000
	3,230T						0	3,230T
	Kg 50,000						0	Kg 50,000
	2,180A						0	2,180A
		2,720T	2,720		21,860		0	27,300T
	18,000 ^{cc}		2,000 ^{cc}				0	20,000 ^{cc}
	Kg 90,000			10,000			0	Kg 100,000
	500g	100g					0	600g
	Kg 6,000						0	Kg 6,000
	Kg 2,000						500g	Kg 2,500
	Kg 10,000						0	Kg 10,000
section	700g						0	700g
	33,400T						0	33,400T

Items	Classification Quantity	Physician	Scientist	✓
Castor oil		Kg 60,000		
Acetophenetidin		Kg 31,000	5,000	
Acetophenetidin tablets		90,000	5,600	
Dextrose		Kg 7,000		
Dextrose injection		9,800 ^A		
Potassium bromide		Kg 7,000		
Bromural		8,000		
Solution of formaldehyde		Kg 158,000		
Mercurachrome		Kg 1,000		
Ether		2,000		
Anesthetic chloroform		4,000		
Ointment of Japan wax		18,000		
Soluble saccharin		6,000		
Iodine		15,000		
Potassium iodide		15,000		
Tincture of iodide Hydrogen Peroxide		15,000		
Hydrous wool fat		60,000		
Zinc sulfate		1,000		
Remijin		3830 ^A		
Scopolia extract		2,000		

N. 4

Classification	Physician	Scientist	Veterinarian	Compound- ing of M.	Retail of M.	Other	Remain- der	Total
Quantity								
	Kg 62,000						18,200	Kg 73,000
	Kg 31,000	5,000	5,000				0	Kg 41,000
	90,000	5,600	5,600				0	101,200 ^T
	Kg 7,000						400 ^g	Kg 7,400
	9,800 ^A		600				0	104,000 ^A
	Kg 7,000						400 ^g	Kg 7,400
	8,000						500 ^g	Kg 8,500
	Kg 158,000						40,000	Kg 198,000
	Kg 1,000						400 ^g	Kg 1,400
	2,000						0	Kg 2,000
	4,000						0	Kg 4,000
	18,000						2,000	Kg 20,000
	6,000						0	Kg 6,000
	15,000						5,000	Kg 20,000
	11,000						5,000	Kg 20,000
	15,000						5,000	Kg 20,000
	60,000		5,000	6,000			0	Kg 71,000
	1,000						200 ^g	Kg 1,200
	3830 ^A						0	38,300
	2,000						0	Kg 2,000

Feb. 16, 1948.

TO : Capt. Lawrence, Ehime Military Govt. Team.
 FROM : Chief of Medicine Sect., Sanitary Dept., Ehime Ken.
 THROUGH: Chief of Liaison Section, Ehime Ken.
 SUBJECT: ~~Change~~ Report on Anaesthetic for Jan., 1948.

I beg to submit to you a report, subject as above.

1. quantity of anaesthetic kept stored at the beginning and the end of this month, including the amount received and released during this month:

Local wholesale dealers (see attached paper).

2. Classification of registered dealers:

Local wholesale dealers:	3
Retailers	75 (decreased by 14)
Consumers	984 (decreased by 52)
Doctor	749
Dentist	216
Veterinarian	19
Drug manufacturer	115
Experimentist ...	1
<u>TOTAL</u>	<u>2,169</u>

3. Confiscated or purchased as evidence.

a. Port and border area.

Conf- fis- cation No.	Place con- fis- cation	Name & age of confis- cation	Occupation.	Reason for confis- cation	Anaesthetic Name : Qt.	Con- fis- cator	Place now stored	Viola- tion number
None								

b. Other areas excluding above a).

i. Registered persons.

Con- fis- cation No.	Place con- fis- cation	Name & age of confis- cation	Occu- pation	Reason for confis- cation	Anaesthetic Name : Qt.	Con- fis- cator	Place now stored	Viola- tion number
None								

ii. Unregistered persons.

None

- 2 -

iii. Total amount confiscated.

None

iv. Anaesthetic purchased as evidence.

None

4. Violation.

a. Registered persons.

None

b. Unregistered persons.

None

5. Decision.

a. Registered persons (inclusive of unconvicted personers).

Decision Number	Occupation Register No.	Name	Decision	Name of court Date decided	Reason for decision	Violation number
	Doctor 133210	MANABE Taketoshi				

6. Toxicosis.

a. Nationality.

	Japanese	Korean	Chinese	Others	Total
Man	68	9	-	-	77
Woman	58	1	-	-	59
Total	126	10	-	-	136

b. Classification.

	Toxicosis	Recovered	Unknown	Others	Total
Man	9	24	29	15	77
Woman	6	23	24	6	59
Total	15	47	53	21	136

c. Anaesthetic.

	Morphin	Heroin	Cocain	Phan to pon	Others	Total
Man	51	4	1	12	9	77
Woman	42	2	-	14	1	59
TOTAL	93	6	1	26	10	136

- 3 -

d. Increase and decrease.

	Increase		Decrease	
	New case:	From other Pref.	Death :	To other Pref.
Man	0	0	0	0
Woman	0	0	0	0

7. Theft. (Unarrested) ~~during November~~

None

Total amount of stolen anaesthetic.

None

8. Lost anaesthetic.

None

FUJITA Ichiro
 Chief of Medicine Section,
 Ehime Ken.

STK

January 1948

Report of local wholesale

Preparations of	Item	Unit	Stock as of 1st of the month	In	
				From central wholesale etc	From commission and retail
Preparations of cocaine	Powdered cocaine hydrochloride	g	615	225	
	Cocaine hydrochloride for injection 1% (1.0%)	A	274		
Preparations of opium	Powdered opium	g	540	300	
	Tablets of opium (0.03g)	T	6900		
	Tincture of opium	g	3000	1250	
	Comphorated tincture of opium	g	175		
	Powder of ipecac and opium	g	1375	2625	
Preparations of opium	Powdered morphine hydrochloride (0.005g)	g	664	525	
	Tablets of morphine hydrochloride 1/40 (1.0%)	T	100		
	Morphine hydrochloride for injection 1/40 (1.0%)	A	8220	5500	
	Atropin morphine for injection	A	1090	1500	
	Ronpas for injection (1.0%)	A	250		
	Ethyl morphine hydrochloride	g	169	90	
Preparations of morphine	Powdered codeine hydrochloride	g	1115	2500	
	Codeine phosphate powder (10%) (0.03g)	g		175	
	Tablets of codeine hydrochloride	T	36850	1000	
	Hydrocodeine phosphate	g	230	50	
	Codeine sulphate	g	105		
	Preparations of Pantopon	Pantopon for injection 2% (0.6%)	A	18	175
" " 2% (1.0%)		A	3000	6000	

Statement of local wholesales in Ehime prefecture (Nov)

Stock as of 1st of the month	IN		out		Stock as of the end of the month	Remarks (No good or cast away)
	From central wh. etc	From consumers and retailers	To consumers and retailers	To others		
615	225	35		205	670	
274				117	157	
540	300			300	540	
6900				600	6300	
2000	1250			1225	2025	
175					175	
1575	2625	50		1225	2825	
664	525			510	679	
100				100	0	
8220	5500			6600	7120	
1090	1500			1020	1570	
250					250	
169	90			59	200	
1115	2500	5		1645	1975	
	175			50	125	
36850	1000			9200	28650	
230	50			195	85	
105				40	65	
18	175	24		36	181	
2000	6000			4650	4350	

January 1948

Report of local wholesales

Item		Unit	Stock as of 1st of the month	From central wholesales etc	In and
Preparations of pantopon	Pantopon for injection ^{2%} (1.1 ^{cc})	A	284		
	Pantopon scopolamin for injection ^{2%} (1.0 ^{cc})	A	7,820	500	
	" " ^{4%} (1.0 ^{cc})	A		1,000	
	" " ^{4%} (1.1 ^{cc})	A	30		
	Pantopon atropin for injection ^{2%} (1.1 ^{cc})	A	12		
	Pantopon papaverin for injection ^{1%} (1.1 ^{cc})	A	710		
Preparations of pavinal	Tablets of Pavinal (0.005g)	T	20		
	Pavinal for injection ^{1%} (1.0 ^{cc})	A	50	400	
	Tablets of Pavinal atropin (0.01g)	T	100		
	Pavinal atropin for injection (1.0 ^{cc})	A	170		
Preparations of cotomin	Tablets of Eustaptin (0.05g)	T	60		
	Eustaptin for injection (1.0 ^{cc})	A	5		
Preparations of tropacocain	Tropacocain hydrochloride	g	5		
	Tropacocain hydrochloride for injection ^{6%} (1.0 ^{cc})	A	120	5	
	" " ^{0%} (1.2 ^{cc})	A		20	
	Apomorphine hydrochloride	g	2		
Tablets of Styptal	T	20			
Antifusten for injection (1.0 ^{cc})	A	700			
Opistan for injection (1.0 ^{cc})	A	3,500	700		
Ticoin for injection (1.0 ^{cc})	A	10			

of local wholesales in E hime prefecture

(NO 2)

Stock as of 1st of the month	In		out		Stock as of the end of the month	Remarks (No good or cast away)
	From central wholes etc	From consumers and retailers	To consumers and retailers	To others		
284				6	278	
7820	500			1510	1710	
	1000			420	580	
30				18	12	
12					12	
710				270	440	
20					20	
50	400			270	180	
100				100	0	
170				80	90	
60					60	
5					5	
5				1	4	
120	5				125	
	20				20	
2					2	
20					20	
700				50	650	
350	700			420	630	
10					10	

January 1948

Report of local wholesales in

Item	Unit	Stock as of 1st of the month	IN	
			From central wholesales	From com and ret
Solution of kaffose	g	1,000	500	
Tablets of opiel	T	314,810		
Solution of opiel	g	1,500		
Powdered opinarcos	g	2,000		
Solution of opinarcos	g	9,500		
Powdered alinda	g	16,500		
Tablets of haburon	T	4,140		
Powdered Sekicil	g	8,000		
Tablets of res-pecton	T	104,400		
Syn-histamin		32,880		
Tenthos		5,700		

Preparations of poppy's hull

Stock of local wholesales in E. hime prefecture

(No. 3)

Stock as of 1st of the month	IN		OUT		Stock as of the end of the month	Remarks (No good or lost away)
	From central wholesales etc	From consumers and retailers	To consumers and retailers	To others		
1.000	500				1.500	
314.810		200		2.800	307.210	
1.500					1.500	
9.000					9.000	
9.500					9.500	
16.500					16.500	
4.140					4.140	
8.000					8.000	
104.400					104.400	
32.880					32.880	
5.700					5.700	

1. Object of the current penicillin research.

The existing equipments were constructed for the purpose of carrying out research works on the culturing and refining processes as well as training researchers and their assistants in penicillin preparing processes.

As is clearly described in the table (ANNEX 1) the facilities have never been operated up to their full capacity all at once from the start, but the volume of charge and the charging frequency per week has been gradually increased step by step to the present status.

While with the view that the substantial production of commercial penicillin could not be carried out by the surface (bottle) culture process (this is the reason why we have been making use of the Erlenmeyer flasks which the company had in hand rather than purchasing flasks by which the space is more efficiently utilized) we had planned the tank (submerge) culture process. Now the construction of penicillin plant is under progress thanks to the kind approval given by GHQ, SCAP and the Ministry of Finance.

However, to meet with the urgent demand of the Ministry of Welfare and also urged by our unquenchable desire to contribute as much as possible to the health and welfare of the people, we decided to operate the existing equipments up to the limit, thus we are exerting the strenuous efforts to increase the charging volume up to 100 liters for daily operation.

For the month of Nov. we have set up our production goal at 1,000 ampules (vials) of 30,000 units content, at the minimum.

2. Re: Penicillin yield.

(A) The yield of the penicillin produced in our plant has not been always satisfactory. The principal reasons for this can be attributed to the facts firstly that it was of the products of the training period for the technicians and workers, and secondly that the facilities were not well completed and fully arranged as they are originally planned. Describing details, there were lack of the refrigerator for the rapid cooling of the cultured broth, lack of filter-press for rapid filtration of broth, lack of the super-cooling refrigerator for the freeze-drying process which prolong the time for the drying process and even make it difficult to maintain the "final rich water" in a frozen state. (the latter case has been temporarily remedied recently by the utilization of dry ice), the inoperable state of the vacuum pump of the freeze-drying process, and lack of measuring apparatus for the high vacuum.

Lately, these aforementioned bottlenecks were almost completely removed and this has brought about a marked improvement of the yield. At present we are exerting further efforts to raise the yield by improving our processing technique.

(B) In determining the yield of the penicillin process, the assay method itself must be brought to the careful scrutiny. In our company, the dilution assay method has been adopted together with the cylinder (cup) method. It is well-known that errors are apt to rise in the dilution method. While on the other, without a reliable standard, penicillin assay by the cup method will not

give accurate results.

However, as we could not so far obtain standard penicillin from the Sanitary Research Institute of the Ministry of Welfare, were obliged to use our product penicillin as the working standard. The sample submitted to the Sanitary Research Institute of the Ministry of Welfare for preliminary assay test shows following results.

Assay by dilution method

(In our assay room) ----- 300 units/mg

Assay by cup method

(Sanitary Research Institute) ----- 97.8 units/mg

Consequently by multiplying 0.33 by the results obtained in our assay room we are likely able to get the correct potency. However, to be strict and safe, the multiplying factor of 0.25 instead of 0.33 has been tentatively adopted until we will be able to ascertain by accurate assay with the standard penicillin.

(C) The figures presented in the Annexed Paper No.1 are those calculated by multiplying 0.25 by the results obtained by the dilution assay method (the figure prior to 25th, Setp. is the result as it is obtained by the dilute assay method). As explained in paragraph (B) the multiplication by 0.25 is rather severe, hence on the annexed table No.2 the figure is presented for your reference calculated by multiplying 0.33 as factor instead of 0.25.

Viewing the production program of the penicillin producing companies in Japan during the period from Nov. to Dec. of this

year (reports submitted to Ministry of Welfare) the volume of broth required for the manufacture of one ampule (30,000 units content) of penicillin is around 0.6 to 5 liters. (By the method of surface culture.) Several companies among these are using *Penicillium chrysogenum* (Q.176) and obtaining 300 units per cubic centimeters therefore the volume of broth required for one ampule (of 300,000 units) could be small. However, inasmuch as several other companies are using the *Penicillium notatum* (NRRL 1978 B.2) and other strains which give broths considerably low in potency, the volume of the broth required for one ampule (of 30,000 units) would be large. Taking these facts into consideration, the consumption of 2 to 4 liters of broth for one ampule of penicillin as in the case of our company cannot necessarily be regarded as poor. However, every effort has been and is being exerted to stop using *Penicillium notatum* (B.2) and to shift it to *Penicillium chrysogenum* (Q.176) instead.

(D) Although the average broth potency for the month of Oct. was 35 units per cubic centimeters, the culture for one charge in our company is usually finished in 5 days compared to 9 to 12 days required in other companies. Taking this into our accounts the potency of broth can be regarded as tantamount to 70 units in the same period of other companies.

(E) As aforementioned, we could not so far obtain the standard Penicillin for assay by cup method which has been causing us much inconveniences in checking the reaction in the cultivation,

refining and other processes because of the lack of accurate potency assay. Fortunately by the negotiation with the Ministry of Welfare and the Japanese Penicillin Research Association, it is understood that we be fortunately shared with standard penicillin for assay use. (Expected to be delivered on 6th of Nov.)

3. Re: Raw materials.

(A) Pepton

Pepton is not being used at present, but in view of the experiment that a minor addition of this substance even to the United States synthetic media showed a favorable results, we have decided to use it before long. Monthly consumption of Pepton with the commencement of the operation of the penicillin plant by the tank (submerge) culture method is estimated 250 to 500 kilograms. (For only surface method 50-100 kgs.)

(B) Butyl-acetate

The present consumption of butyl-acetate is minor as we are now refining the penicillin by utilizing active carbon but in case we could acquire a sufficient supply, we are desirous to shift it to the direct extraction by butyl-acetate.

(C) Lactose

Difficult to procure.

4. Re: Equipments

The various shortcomings kindly pointed out by you will be immediately remedied.

5. Re: Disposition of the finished products.

As we had not received the legal assay tests (such as of its sterility, toxicity, pyrogens and etc.) from the Sanitary Research

Institute of Ministry of Welfare, we are strictly refraining from using it on human bodies.

Before long the toxicity and pyrogens test will be entrusted to the Microbiological Research Institute of the Osaka University. Under these circumstances all the penicillin products, except those used for assay sample as mentioned in paragraph 2 (B) and the working standards for the cup method and samples to check refining process, are stored ~~sa~~safely in our hands as indicated in annexed table 3.

Chronological Outline of
Research on
Penicillin Manufacturing Process

Nissin Chemical Co., Ltd.

- In Feb. 1944, Commenced study for fungi of good penicillin producing ability.
- In Mar. 1944, Commenced experimental research on the penicillin process, principally bacteriological research for a new micro-organism.
- In Mar. 1946, Three penicillin producing strains (No.233, G1 and No.176) and one assay test bacterium (Staphylococcus Aureus Terajima) were transferred to us from the Faculty of Agriculture, Tokyo University, and also two assay test bacteria (Staphylococcus Aureus Terajima and St. A. Hestley) from the Faculty of Agriculture, Kyushu University, which enabled us to carry out comparative tests of the isolated strains and their penicillin producing abilities.
- In June 1946, Started research on the process of preparing penicillin on an industrial scale.
- In Sept.1946, Constructions of a culture room and refining room were completed.
- In Oct. 1946, Commenced research on the process of penicillin refining, and in order to supply it with penicillin broths, started to produce 15 to 20 liters of culture per week as our goal.

- In Dec. 1946, Received two United States' strains (B2 and Q176) tanks to Docter Foster, Penicillin Consultant, Supply Division, SCAP.
- In Jan. 1947, Completed construction of the culture room of surface (bottle) process capacity of which was 100 liters per day.
- In Feb. 1947, Commenced our experimental production of 10 liters per charge and 5 charges per week by the surface (bottle) culture process. Installed apparatus for shaking culture.
- In Mar. 1947, Applied to GHQ, SCAP through the Ministry of Finance for the approval for borrowing funds (7,000,000 Yen) for the construction of the penicillin plant by tank process.
- In Apr. 1947, Started enlargement of experimental production by the surface (bottle) method to the extent of preparing 20 liters per charge and 5 charges a week.
- In July 1947, Took primary procedures for an enlargement (to the extent of preparing 70 liters per charge and 5 charges a week) of experimental production by the surface (bottle) culture method.
- In Aug. 1947, The application asking for permission for borrowing funds was approved by AG 095 (28 July '47) ESS/AG (SCAPIN 4231-A). Embarked on installation of facilities for preliminary tests by the tank (submerged) method, i.e.. 1 fermenter of 250 liter-size, and also

commenced preliminary construction work of our penicillin plant.

In Sept. 1947, Submitted a part of experimentally produced penicillin to Sanitary Research Institute of the Welfare Ministry asking for its potency assay test, and although it was 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 Sept. 27th is shown in annexed copies of laboratory's date and receipt book were temporarily corrected as shown within parenthesis.)

In Oct. 1947, Embarked on an enlargement of the experimental production with the aim of treating 50 liters of culture per day.

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

COPY
OF
RECEIPT BOOK

Nissin Chemical Co., Ltd.

Date received	Units received	Date prepared	Units withdrawn	Date prepared	Units on hand
((Ca-salt) (1) (Na-salt)	64,500 (16,125) 106,000 (26,500)	Total units up to June 26			64,500 (16,125) 170,500 (42,625)
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	121,601 (30,400)	3			964,101 (241,025)
8	236,225 (59,056)	7			1,200,326 (300,081)
14	520,000 (130,000)	14			1,720,326 (430,081)
18	384,000 (96,000)	18			2,104,326 (526,081)
21	216,000 (54,000)	21			2,320,326 (580,081)
24	190,000 (47,500)	24			2,510,326 (627,581)
27	231,000 (57,750)	27			2,741,326 (685,331)
30	267,000 (66,750)	30			3,008,326 (752,081)
Aug. 3	359,000 (89,750)	Aug. 3			3,367,326 (841,831)
8	282,000 (70,500)	8			3,649,326 (912,331)

775013

Date received	Units received	Date prepared	Units withdrawn	Date prepared	Units on hand
Aug. 12	253,000 (63,250)	Aug. 12			3,902,326 (975,181)
15	153,000 (38,250)	15			4,055,326 (1,013,831)
19	77,200 (19,300)	19			4,132,526 (103,131)
22	373,000 (93,250)	22			4,505,526 (1,126,381)
25	193,000 (48,250)	25			4,698,526 (1,174,631)
29	323,000 (80,750)	29			5,021,526 (1,255,381)
Sept. 3	119,000 (29,750)	Sept. 3			5,140,526 (1,285,131)
5	199,000 (49,750)	5			5,339,526 (1,334,881)
15	58,500 (14,625)	15			5,398,026 (1,349,506)
22	585,000 (146,250)	22			5,983,026 (1,495,756)
23	62,900 (13,225)	23			6,035,926 (1,508,981)
25	17,200 (4,300)	25			6,053,126 (1,513,281)
30	44,300	30			(1,557,581)
Oct. 1	19,100	Oct. 1			(1,576,681)
2	4,820	2			(1,581,501)
3	19,500	3			(1,601,001)
5	136,700	5			(1,737,701)

Date received	Units received	Date prepared	Units withdrawn	Date prepared	Units on hand
Oct. 6	237,000	Oct. 6			(1,974,701)
7	41,700	7			(2,016,401)
8	189,500	8			(2,205,901)
9			373,000 (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 (54,000)	June 27	
			456,000 (114,000)	July 1	
			359,000 (89,750)	Aug. 3	
			231,000 (57,750)	July 27	
			267,000 (66,750)	30	
			282,000 (70,500)	Aug. 6	
					x As working standard.
Oct. 10	42,000	Oct. 10			(1,659,901)
11			x 189,500	Oct. 8	(1,701,901)
13	202,000	10			(1,512,401)
					(1,714,401)

775013

Date received	Units received	Date prepared	Units withdrawn	Date prepared	Units on hand
Oct. 14			384,000 (96,000)	July 18	As sample for experiments in the refining process.
			585,000 (146,250)	Sept. 22	
			136,700	Oct. 5	
			237,000	6	
14					(1,098,451)
19	243,000	Oct. 19			(1,341,451)
20	920,000	20			(2,261,451)
21	158,000	21			(2,419,451)
			202,000	Oct. 13	For refining experiments. Vial broken.
			253,000 (63,250)	Aug. 12	
			19,500	Oct. 3	As display sample.
23	57,500	23			(2,134,701)
24	41,500	24			(2,192,201)
25	294,000	25			(2,233,701)
26	157,000	26			(2,527,701)
					(2,684,701)

Date received	Units received	Date prepared	Units withdrawn	Date prepared	Units on hand
Oct. 27	375,000	Oct. 27			(3,059,701)
28	653,000	28			(3,712,701)
29	378,000	29			(4,090,701)
30	320,000	30			(4,410,701)
31	268,000	31			(4,678,701)
Nov. 1	203,500	1			(4,882,201)
2	344,000	2			(5,226,201)
4	300,000	4			(5,526,201)
6	284,000	6			(5,810,201)
7	422,000	7			(6,232,201)
8	1,750,000	8			(7,982,201)
9	568,000	9			(8,550,201)
10	1,040,000	10			(9,590,201)
11			653,000	Oct. 28	
			378,000	29	(8,559,201)

Date received	Units received	Date prepared	Units withdrawn	Date prepared	Units on hand
Nov. 12	1,405,000	Nov. 12			(9,964,201)
14	817,000	14			(10,781,201)

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

(Potency units prior to Sept. 30) $\times \frac{1}{4}$

ANNEX 2

Date charged	Volume of broth (liter)	Total powder penicillin (units)	No. of Vials (per 50,000 Units)	Volume broth per vial (liter)
Oct. 1	23	25,470	0.8	27
2	20	6,430	0.2	100
5	35	102,300	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	1.9	19.4
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

775013

ANNEX 1

Laboratory Date
of
penicillin production

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)		
F - 10	Feb. 12	9	7	20 (5)	24,000 (6,000)	17	113 (28)	* 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.
F - 11	13	8.5	7	25 (3)	5,760 (1,440)	5.7	100 (25)	
F - 12	19	6	4	30 (7.5)	25,000 (6,250)	21	254 (63.5)	
F - 13	25	9	7	50 (12.5)	43,200 (10,800)	12.4	370 (92.5)	
F - 14	27	12.3	3.5 (10)	15 (4)	5,300 (1,325)	over 7.1	over 57 (14.5)	
F - 15	March 2	11	8.5	10 (2.5)	25,960 (6,490)	30.5	407 (101.7)	
F - 16	7	13	11	20 (5)	52,000 (13,000)	23.6	122 (30.5)	
F - 17	10	13	9.5	20 (5)	63,500 (20,875)	43.9	260 (65)	