

variation stated above, using the mice reproduction system for vaccine material of this country.

3. Conversion from Harem System to Mated System

Taking the historic course on the improvement of test animals in our country (various problems have been studied and solved centering around dd strain) into consideration, stepwise improvement should be planned laying stress on mice that RSHI has kept breeding since its opening (1927), and it should probably be considered to convert the way of breeding from the Harem system to a mated system.

In the present condition, breeding is continued by using suitable scores of Harems which are large cages about 40x60 cm² wide that ca. 10 female mice and a few male mice are in each.

To secure parent mice for the mated system, pregnant mice estimated to bare on Tuesday in the planned week are selected by interception from the outside, and they are separated one by one into individual cages, when the Harem each mouse is selected from is checked for fear of inbreeding. On Tuesday the female mice in each individual cage is checked if they have bared or not, and it is desirable to select 1 Litter from each Harem, 6 Litters altogether, to give Family names of A,B,C,D,E and F and to control by each Litter afterwards.

Delactate on Tuesday three weeks after birth, and at the same time, separate by sex and give new children names as below:

Family name :	A	B	C	D	E	F
Male Children :	Ad	Ae	Aa	Af	Ac	Ab (male spare parent)

Select one mouse from a cage of each sex on Wednesday seven weeks after birth and put six couples as $\Delta a + +a \rightarrow A$, $\Delta f + +f \rightarrow F$ together in individual cages and give new family names. Make new Families with the same procedure eight weeks and nine weeks after birth. Proceed to Continuous Mated Breeding System (Fig. 1).

4. A Weekly Work Schedule for Continuous Mated Breeding

This breeding system, making a more systematic production of mice possible, requires a rational work plan. Shown here is an example of weekly work schedule according to Takeda System which makes daily work as dispersed as possible and has a great degree of freedom around the date of birth, taking elimination of labor into consideration.

Fig. 1 Schedule on Fertilization, Birth, Ablactation and Supply in Continuous Mated Breeding System (rejected after the eighth birth and ablactation)

Weeks after mating	Number of Birth							
	1st birth	2nd birth	3rd birth	4th birth	5th birth	6th birth	7th birth	8th birth
0	Fertilization 1							
1								
2								
3	Birth	Fertilization 2						
4								
5								
6	Ablactation and Supply	Birth	Fertilization 3					
7								
8								
9	Ablactation and Supply		Birth	Fertilization 4				
10								
11								
12	Ablactation and Supply			Birth	Fertilization 5			
13								
14								
15	Ablactation and Supply				Birth	Fertilization 6		
16								
17								
18	Ablactation and Supply					Birth	Fertilization 7	
19								
20								
21	Ablactation and Supply						Birth	Fertilization 8
22								
23								
24	Ablactation and Supply							Birth
25								
26								
27								
28	Ablactation and Supply							

(1) Monday: weekly preparations

Cage, Water Supply Bottle, Shaving, Breeding Stand, Ticket, etc.

(Example for Ticket)

Family name			
Date of mating			
Date of birth	Size of litter	Date of weaning	Remarks

Staff Meeting, Recording, and Filing, etc.

(2) Tuesday: check of born mouse

Put a birth cage on a working bench → Check the number of the baby mice → Write down the date of birth and Litter size on a Ticket → Attach age Color cards → Put back on the breeding stand.

(example of Color card)

Age of baby mouse (week)	1	2	3	4	6	7
Parent pregnancy days	1 - 7	8 - 14	15 - 21	1 - 7	8 - 14	15 - 21
Color card	red	green	yellow	red	green	yellow

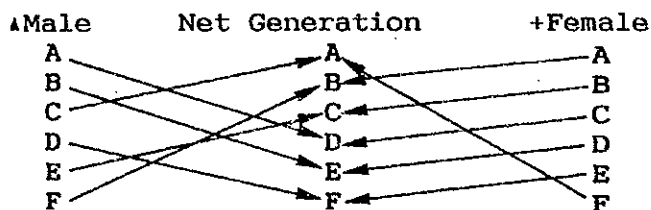
(3) Wednesday: putting male and female together (mating)

Prepare cages and a breeding shelf → Select one male and one female of the same code name from

spare parent groups (♂Children, ♀Children: older than seven weeks) and make a new cage of next generation → Write in a Ticket according to the form → Confirm water and feed supply → Put the cages back to the shelf.

(Reference: a basic combination of

Random Rotating System composed of 6 groups)



(4) Thursday: Ablactation --- Preparation (a tray for ablactation, a new cage, Sawdust) → Transfer parent mice to the new cage → Check the sex of the mouse to ablactate → Classify by sex and put into the cage Supply --- Preparation (a cage for supply) → Supply mice of 4 weeks old → Check the sex and weight (7 - 14 gr.) of the mice → Record the sex and weight on the cage.

(5) Friday: Exchange of cages (1.5 weeks old) --- Preparation (a new cage) → Transfer parents and the baby mouse of 1.5 weeks old to a new cage → Put back to the breeding shelf.

Washing a cage --- Dump the filth in the cage → Soak the cage in warm water for 10 to 20 minutes → Wash the cage → Dry.

Feeding --- Add to the feeder whose baits have

decreased. (usually 300 gr.)

5. Systematic Production of Mice through Continuous Mated System

To identify genes of an RS impure line as far as possible, I have explained assuming Random Rotating System for breeding. Therefore what plan is suitable has been considered to produce mice by this system.

(1) Preparation of Parent Mice

The course from the first birth to rejection of parent mice has been shown in Fig. 1. For Random Rotating, six pairs of parent mice are one production unit. Three units running with one week difference can supply ca. 60 mice every week. Making this production group as a basis, parent mice can be systematically prepared according to the number of mice required in a week (Miniature 2).

(2) Breeding and Supply Plan

Miniature 3 shows a model of breeding and a supply plan to respond to the continuous demand. These plans indicate that the RS impure line can be continuously supplied by week from the fifteen weeks after conversion to the mated system. The least supply unit is ca. 240 (18 cages) in a month. Therefore when we have four ordinary breeding shelves and 1144 pairs of parents, we will be able to ship ca. 2,000 mice in a month at best.

6. Investigation on Efficiency of Breeding, Economical Efficiency and Demand

On the efficiency of breeding in the continuous mated breed-

ing system with an RS impure line, investigate on the following items:

- (1) Rate of pregnancy
- (2) Period of pregnancy
- (3) Childbearing days
- (4) Litter size
- (5) Ablactation rate
- (6) Weight increase
- (7) Immunological ability
- (8) Toxicity reaction

Fig. 2 (Miniature) Preparation of Parent Mice in Continuous Mated System

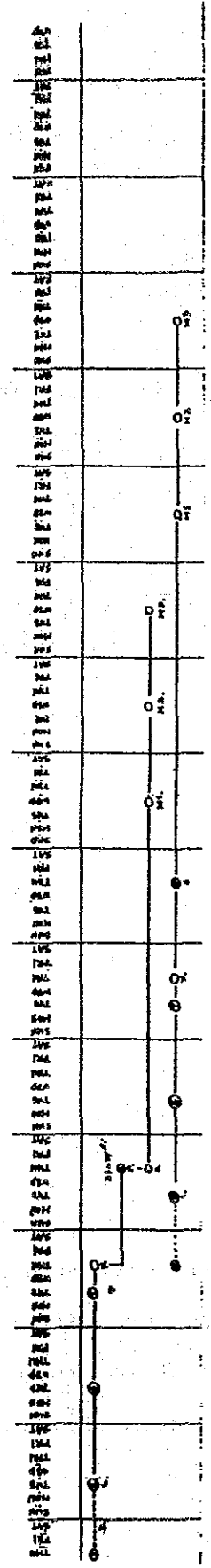
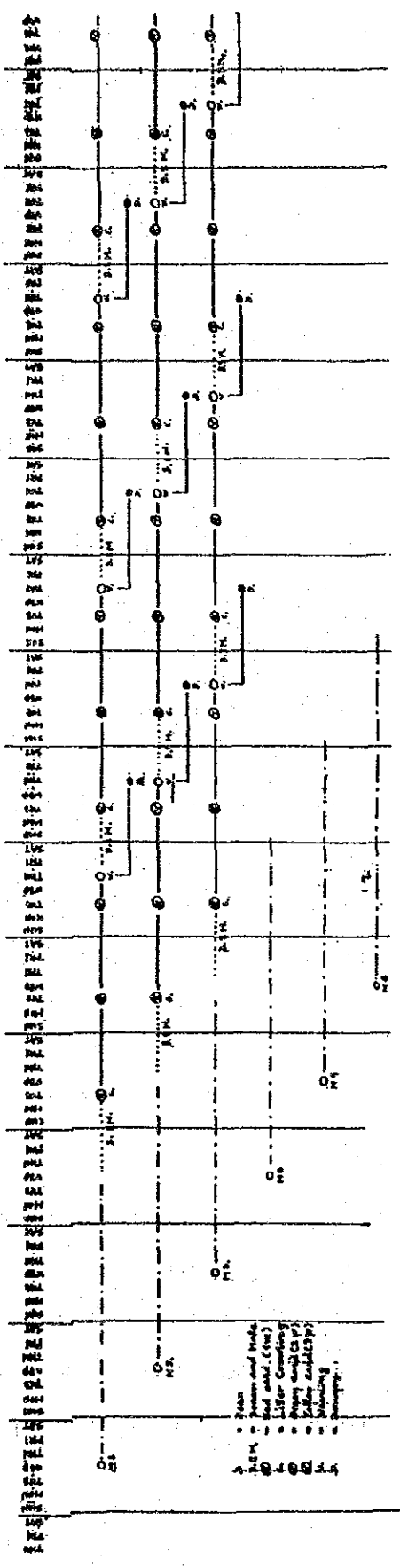


Fig. 3 (Miniature) Schedule of Production of Mice in Continuous Mated System



To grasp the economic efficiency (production costs) of the new breeding system, investigate the following items:

- (1) Investigation of actual facts of old Harem system
 - (a) actual conditions of production
 - (b) parent mice --- male/female ratio, current number, age counted by week, and weight
 - (c) pregnancy rate
 - (d) ablactation --- ablactation rate, sex ratio, weight, disease, and Litter size
 - (e) actual supply
 - (f) production capacity of Farm
- (2) Investigation of costs of the new system
 - (a) facility costs
 - (b) labor costs
 - (c) service costs
 - (d) cost of feed
 - (e) supplementary material costs
 - (f) other expenses
- (3) Investigation of source of funds for production of mice
 - (a) budget
 - (b) income
 - (c) investment
 - (d) running costs
 - (e) immaterial profits and others

At the last, compare the economical efficiency of both the new and the old system with production costs and others.

On the other hand, the important point to regard is the equalization of demand and supply. To attain it, it will be

necessary to develop as many customers as possible to increase the capacity of controlling supply, and to secure customers to accept surplus animals. Here, investigate the following items for it:

- (1) The producers investigate big customers to supply the same type but different kind of mice and grasp the users of mice.
- (2) Investigate the actual conditions of market demand and supply with questionnaires by mail:
 - (a) amount of mice to use
 - (b) supplier
 - (c) degree of satisfaction about quality
 - (d) request
 - (e) others

7. Introduction of Disease Check System

It is necessary to investigate on the actual conditions of disease with RS hybrid colonies. To begin with, perform next tests:

- (1) Pathological Oral Medication Test --- pneumonia, hepatitis, lymph node swelling, etc.
- (2) Parasite Test --- Syphcia oxuritis, Hymenolepcis, etc.
- (3) Serological Test --- HVJ, MHV, etc.
- (4) Bacteriological Test --- Tizzer disease, etc.
- (5) Pathologic Histological Test
- (6) Virological Test, etc.

Establish a test system for infectious diseases of mice

shown in Table 1 step by step.

8. Introduction of Germ-free Mice

Control of germ-free mice is a basic technique for introduction of Specific Pathogen-free (SPF) mice.

Import existing germ-free mice (BALB/c strain for substantial use), prepare a few vinyl plastic isolators and aim at learning the techniques of feeding, sterilization, barrier system and Foster mother manipulation, etc. It may be significant enough as a negative control of disease test in Section 7.

9. Introduction of SPF Mouse

SPF mice are a mouse colony which have germ-free mice as ancestors and have no infectious diseases in Table 1. They are bred in a barrier system. A barrier system is made up of following techniques:

- (1) Fumigation with gas
- (2) Maintenance of higher pressure with sterilized air (using High Efficiency Particular Air Filter)
- (3) Use of Pass Room for human body (divestment, washing with shower, sterilized cloth)
- (4) Use of Pass Room for things (with a double-door autoclave and an EO gas sterilizer)
- (5) Use of Pass Room for things (sterilization room for transfer of things and animals)
- (6) Sterilization of supplementary material for feeding such as solid feed and Litter.

A plane figure of a building for Barrier system is shown in

Fig. 4 as an example.

10. Introduction of Strain Mouse and Learning Genetic Test Technique

Plan for introduction of DD strain as a common mouse strain and BALB/c, C3H/Hc, C57BL/6, ICR for special purposes. Make an RS impure line SPF by Foster mother breeding of baby mice extirpated by cesarean section, using germ-free mice, and check the characteristics.

That is all. (Oct. 13, 1993)

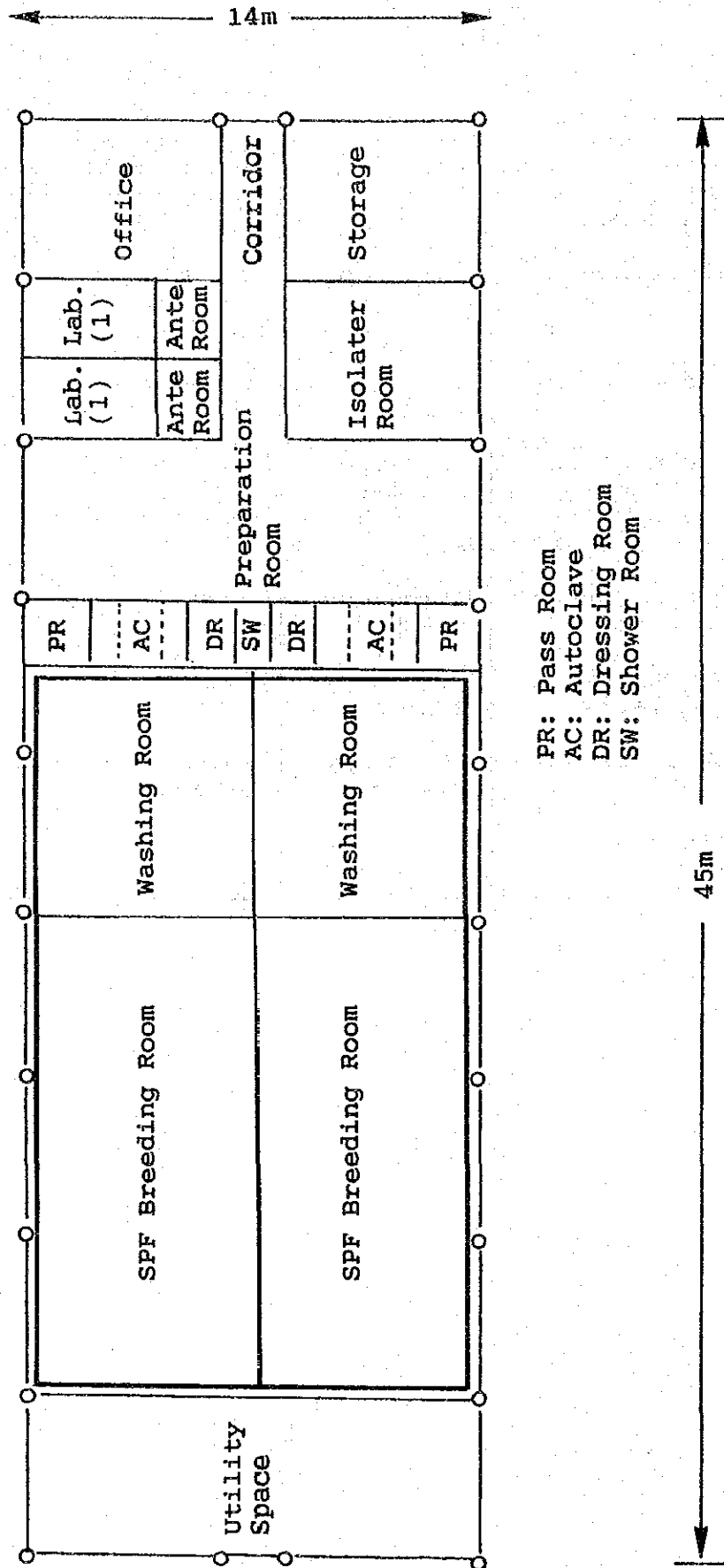
Table 1. Name and Checking Method of Specific Pathogen of Mice

(WHO : 1979)

Name of Pathogen	Check Method	Check Materials	Remarks
Bacteria			
<i>Pseudomonas aeruginosa</i>	Culture	Caecum, Skin, Abscess	NAC media
<i>Salmonella</i> spp	Culture	Caecum, Lymphnode, Region of Liver & Spleen	DHL, Harnar media
<i>Escherichia coli</i> 0115a,c:K(B)	Culture	Caecum	DHL media
<i>Pasteurella pneumotropica</i>	Culture	Pharynx - Larynx Region of Lung	Blood agar media
<i>Corynebacterium Kutscheri</i>	Culture Serological ex.	Oral, Caecum, Serum, Region of Liver Spleen, Kidney	FNC media, Agg.
<i>Bacillus piliformis</i>	Microscopy of smear serological ex.	Necrotic Region of Liver, Heart, Serum	IFA, Giwsa, stain
<i>Mycoplasma pulmonis</i>	Culture Serological ex.	Oral cavity Trachea, Serum Region of Lung	PPLO, ELISA CF
Virus			
Sendai virus (HVJ)	Serological ex.	Serum	ELISA, CF HI
Mouse hepatitis virus (MHV)	Serological ex.	Serum	ELISA
Rotavirus	Serological ex.	Serum	HI
Mouse adenovirus	Serological ex.	Serum	CF
Reovirus type 3	Serological ex.	Serum	CF

Name of Pathogen	Check Method	Check Materials	Remarks
Protozoa			
Eimeria spp	Microscopy of smear	Caecum	Saturated Sucrose, salt soln
Girardia muris	Microscopy of smear	Duodeum	Protozoa
Spiro nucleus muris (Hexamita)	Microscopy of smear	Duodeum	Protozoa
Parasite (iut.ext)			
Syphcia spp	Microscopy of smear	Caecum, Anus	Worm, Egg
Cysticercus fasciolaris	Microscopy of smear	Liver	Worm
Myobia musculi	Microscopy of smear	Region of Body-surface	Worm, Egg
Radfordia affinis			

Fig. 4 Model of Animal Breeding Facility.



L A W N O : 3 9 5 9

LAW REGARDING ESTABLISHMENT OF HYGIENE CENTER
OF TURKISH REPUBLIC (*)

30 January 1940

(Issue date in the Government News paper: 4 January 1941, No.4703)

3. t. Norm v.22 - p 85

Article 1 - Central Hygiene Institute which has been established as a Hygiene Institute and Hygiene school, under the responsibility of the Ministry of Health and Social Aid is obliged to carry out the duties which have been outlined in this law. (*)

Hygiene Institute may open up new hygiene institutes as the Ministry of Health and social aid require according to the needs of the various regions of the country.

Hygiene Institute

Article 2 - Hygiene Institute is divided into various specialization branches by the Ministry of Health and social Aid.

This institution is responsible for following as the Ministry requires:

A)To carry out health and hygienic researches to protect the public against all kinds of Diseases.

B)To prepare sera, vaccines and various biological and chemical substances of which the kinds were determined by the Ministry.

C)To control local or imported vaccines, sera and chemicals according to relevant laws.

D)To purchase and control the items which are written in the Clauses a, b, c and d of Article 2 and 10 of Law No. 1262 Pharmaceutical and Medical Prepareds.

E)To hold conferences or publish documents on general, social or various matters.

(*)Alteration of Name, Hygiene Institute and Hygiene School, Turkish Republic Refik Saydam Central Hygiene Institute since 10 Aug. 1942,

(現在 : Refik Saydam Hygiene Center Presidency)

181 sayılı Kanun 3. maddesi
beşerî kuruluş aldatılmı ve f...
P. S. M. K. Kurta, 1983

hinden itibaren üç ay zarfında müracaat ettikleri takdirde yalnız imtihana tabi tutulurlar. Bunlar imtihan neticesine kadar san'atlarını icraya devam edebilirler. İmtihanda muvaffak olanlara bir gözlükçülük ruhsatnamesi verilir.

İkinci Muvakkat Madde — Bu kanun neşri tarihinde en az on senedenberi bir ticarethane açmış olarak veya eczanesinde gözlükçülük yaptıkları, mahallin en büyük mülkiye amiri tarafından verilmiş bir vesika ile sabit olanlar, bu kanunun birinci maddesinin 1, 2 ve 3 üncü fıkralarında yazılı şartları halz olmasalar bile sanatlarını icraya devam ederler.

Birinci fıkrada yazılı şartları halz olanlara kanunun mer'iyeti tarihinden üç ay zarfında müracaat ettikleri takdirde Sıhhat ve İçtimai Muavenet Vekâleti tarafından bir ruhsatname verilir.

Madde 17 — Bu kanun neşri tarihinden üç ay sonra mer'idir.

Madde 18 — Bu kanunun hükümlerini icraya Adliye, Dahiliye, Maliye ve Sıhhat ve İçtimai Muavenet Vekilleri memurdur.

—oO—

KANUN NO: 3959

4-1-1941

TÜRKİYE CUMHURİYETİ MERKEZ HIFZISSIHHA MÜESSESESİ
TEŞKİLİNE DAİR KANUN (*)

39 Kanunvevel 1941

[Resmî Gazete ile neşir ve İlanı: 4 Kanunusani 1941 — Sayı: 4703]

3. t. Dâstur, c. 23 — n. 86

Madde 1 — Sıhhat ve İçtimai Muavenet Vekâletine bağli, Hifzıssıhha Enstitüsü ve Hifzıssıhha Mektebinden ibaret olmak üzere teşkil edilen (Türkiye Cumhuriyeti Merkez Hifzıssıhha Müessesesi) bu kanunda yazılı işleri yapmakla mükelleftir. (*)

Memleketin muhtelif mıntakalarının sıhhi ihtiyaçlarına göre Sıhhat ve İçtimai Muavenet Vekâletinin göreceği lüzum üzerine aynı işleri yapmakla mükellef enstitü şubeleri açılabilir.

Hifzıssıhha Enstitüsü

Madde 2 — Hifzıssıhha Enstitüsü Sıhhat ve İçtimai Muavenet Vekâletince muhtelif ihtisas şubelerine ayrılır.

Bu müessese vekâletçe gösterilecek lüzum üzerine:

A) Halk Hifzıssıhha şartlarının ıslah ve inkişafına ve her nevi hastalıklarla mücadelede yarayacak sıhhi ve fenni araştırmaları ve incelemeleri yapmak,

B) Vekâletçe nevlere tayin edilen serum ve aşuları ve sair biyolojik ve kimya maddelerini hazırlamak,

(*) Müessesenin adı, 10.8.1942 tarih ve 4288 sayılı kanunla (TÜRKİYE CUMHURİYETİ BEKİK SAYDAI MERKEZ HIFZISSIHHA MÜESSESESİ) olarak değiştirilmiştir.

C) Hususî kanunlarına tevfikân yerli veyahut yabancı müstahzarların, serumı ve aşılarda sair hayattî tertip veya kimyevî maddelerin kontrollerini yapmak,

D) 1262 sayılı İspençiyarî ve Tıbbî Müstahzarlar Kanununun 10 uncu maddesine göre daimî murakabeye tabî tutulan İspençiyarî ve tıbbî müstahzarat ile mezkûr kanunun ilâncî maddesinin a, b, c ve d fıkralarında yazılı maddeleri satın alarak İcap eden muayenelerini yapmak;

E) Umumî ve İctimatî Hıfzıssıhaya ve sair mevzulara ait konferanslar tertip etmek ve neşriyat yapmaktaki mükelleftir.

Maddo 3 — Hıfzıssıhha Enstitüsü ihtisas ve salâhıyeti dahilindeki fennî ve sıhhi meseleler hakkında resmî daireler ve belediyelerle hakikî ve hükimî şahıslar tarafından doğrudan doğruya vukubulacak talep ve müracaatları kabul ederek bunlar üzerinde tetkikler ve İcap eden tahlil ve muayeneleri yapar ve reyini ve mütalâasını bildirir.

Maddo 4 — Hıfzıssıhha Enstitüsü vazifesi arasında sayılan tetkik ve muayene ve tahlillerden umumî sıhhat taallûk eden işler için resmî daireler ile belediyelerden hiçbir ücret almaz. Umumî sıhhat taallûk etmiyen muayene, tahlil ve tetkikler için alınacak ücretler Sıhhat ve İctimatî Muavenet Vekâletince hazırlanarak İcra Vekilleri Heyetince tasdik edilen bir tarife ile tesbit edilir. Sarı veya salgın hastalıklar işleri müstesna olmak üzere hakikî veya hükimî şahıslara ait olan muayene, tahlil ve tetkikler de aynı tarife üzerinden ücrete tabidir.

Maddo 5 — Enstitüde hazırlanan her nevi aşı ve serum ve diğer maddelerin satış kıymetleri ile bunların ne suretle satışa çıkarılacakları ve bunları toptan ve perakende olarak satanlara verilecek bey'îye miktarı Sıhhat ve İctimatî Muavenet Vekâletinin teklifi üzerine İcra Vekilleri Heyetince tâyin edilir.

Maddo 6 — Hıfzıssıhha Enstitüsü fennî tetkikat ve istihsalâtı için lâzım olan her nevi hayvanları ve yemleri tedarik edebileceği gibi bunları yetiştirmek ve işlerine yarıyacak ekimleri yapmak üzere tesîsat da vücude getirebilir.

Hıfzıssıhha Mektebi

Maddo 7 — Hıfzıssıhha Mektebi Sıhhat ve İctimatî Muavenet Vekâletinin göreceği lüzum ve tertip edeceği program üzerine tababet ve şubeleri sanatlari mensupları ile cezaci ve kimyagerlere ve küçük sıhhat memurlarına umumî ve ferdi hıfzıssıhhaya veya bunlardan memur olanların sıhhi ve fennî ve idari vazifelerine ait amelî ve nazari tekâmül tedrisatı yapmak ve aklîmum ilmi mevzulara ait konferanslar tertip etmek ve neşriyat yapmaktaki mükelleftir.

Tababet ve şubeleri sanatlari mensupları ile cezaci ve kimyagerler ve küçük sıhhat memurlarından Devlet ve belediyelerle bunlara bağı idare ve müesseseler hizmetinde bulunanlar Sıhhat ve İctimatî Muavenet Vekâleti ile alakalı vekâletler tarafından müştereken tesbit edilecek zaman ve sıralarda tekâmül tedrisatında hazır bulunmağa mecburdurlar.

Maddo 8 — Alakalı vekâletler ile Sıhhat ve İctimatî Muavenet Vekâleti tarafından müştereken tâyin olunacak şekil ve sıra ve adetler dahilinde olmak suretiyle

JICA

