6. ASEAN-GMPガイドライン

GOOD MANUFACTURING PRACTICE

GENERAL GUIDELINES

TABLE OF CONTENTS

GOOD MANUFACTURING PRACTICE

GENERAL GUIDELINES

1. INTRODUCTION

1.1 In the manufacture of drugs, overall control is essential to ensure that the consumer receives drugs of high quality.

Haphazard operations cannot be permitted in the manufacture of substances that may be necessary to save life or to restore or preserve health.

The good practices outlined below should be considered as general guides; whenever necessary, they may be adapted to meet individual needs, provided the established standards of drug quality are still achieved.

1.2 The manufacture of drugs depends on the starting materials, manufacturing processes, building, equipment and personnel involved.

It is not sufficient that the finished product passes testing protocols, but quality must be built into the product.

1.3 All drugs should be manufactured under carefully controlled and monitored conditions, and sole reliance should not be placed on any test for assurance of the quality of the end product.

1.4 The purpose of this guide is to outline steps which should be taken, as necessary and appropriate, by manufacturers of drug products with the object of ensuring that their products are of the nature and quality intended. Methods other than those described but which achieve the same ends may be equally acceptable.

2. DEFINITION

For the purposes of this guideline, the following definitions are adopted :

2.01 Batch

A quantity of any drug product produced during a given cycle of manufacture and from a specific formulation order, that is uniform in character and quality (the essence of manufacturing batch is its homogenity).

2.02 Batch Number

A designation (in numbers, letters and or symbols) that identifies the batch, and that permits the complete history of the batch, including all stages of production, control and distribution, to be traced and reviewed.

2.03 Bulk Product

Any processed material in loose form which must, in order to become a finished product, undergo the packaging operation.

2.04 Clean Room or Clean Area

A room or area with defined environmental control of particulate and microbial contamination, constructed, equipped and used in such a way as to reduce the introduction, generation and retention of contaminants within the area.

2.05 Date of Manufacture

A date fixed for the individual batch, indicating the completion date of the manufacture.

2.06 Drug product

Any substance or mixture of substances that is manufactured, sold, offered for sale, or presented for use in (1) the treatment, mitigation, prevention, or diagnosis of disease, an abnormal physical state, or the symptoms thereof in man or animal; or (2) the restoration correction, or modification of organic functions in man or animal.

2:07 Expiration Date or Expiry Date

A date fixed for each individual batch before which the batch still meets the required standard specifications for quality.

2:08 Finished Product

A drug product which has undergone all the stages of manufacturing operations.

2.09 Good Manufacturing Practices or GMP

That part of Quality Assurance aimed at ensuring that products are consistently manufactured to a previously specified quality. It is thus concerned with both Production and Quality Control procedures.

2:10 In Process Control

Checks and tests instituted by the manufacturer and carried out in the course of the manufacture of a drug.

2.11 Intermediate product

Any substance or mixture of substances to undergo one or more stages of processing to become a bulk product.

2.12 Lot

Lot means a batch, or a specific identified portion of a batch, having uniform character and quality within specified limits; or, in the case of a drug product produced by contineous process, it is a specific identified amount produced in a unit of time or quality in a manner that assures its having uniform character and quality within specified limits.

2.13 Lot number or control number

"Lot number" or "control number" means any distinctive combination of letters or numbers, or both, by which the complete history of the manufacture, control, packaging and distribution of a batch or lot of a drug is determined.

2.14 Manufacture or Manufacturing

The complete cycle of production and quality control of a medicinal product from the acquisition of all materials through all processing and subsequent packaging to the despatch of the finished product (unless the context otherwise requires, manufacture includes packaging).

2.15 Packaging

That part of production cycle starting from bulk product filled into containers, labeled and packed.

2.16 Packaging materials

All materials used in packaging and labeling process; containers, closures, bags, packings, label materials (labels, inserts, etc.), seals binding materials, adhesives and tapes.

2.17 Processing

That part of production cycle starting from weighing, compounding of raw materials to the bulk product.

2.18 Production

All operations ranging from processing to packaging.

2.19 Quality Assurance

The sum total of the organised arrangements made with the object of ensuring that products will be of the quality which meet the required standard specification.

It is Good Manufacturing Practice plus factors outside the scope of this Guide (e.g. original product design and development).

2.20 Quality Control

All measures taken during manufacturing, designed to ensure the uniform output of drug products that conform to established specification of identity, strength, purity and other characteristics.

2.21 Quarantine

The status of materials or products set apart (physically or by system) while awaiting a decision on their suitability for processing, packaging or distribution.

2.22 Raw Materials

All substances whether active or inactive whether they remain unchanged or become altered, that are employed in the processing of drugs although not all raw materials necessarily remain in the bulk product.

2.23 Rejected

The status of materials or products which are not permitted to be used for processing, packaging or distribution and should be discarded in a safe manner.

2.24 Released or Passed

The status of materials or products which are permitted to be used for processing, packaging or distribution.

2.25 Representative Sample

A sample that consists of a number of units that are drawn based on rational criteria such as random sampling and intended to assure that the sample accurately portrays the batch or the total amount of materials being sampled.

2.26 Sanitation

Hygienic control on manufacturing processes, including personnel, premises, equipment and material handling (from starting materials to finished product).

2.27 Starting Materials

Both raw materials and packaging materials.

2.28 Sterilisation

Inactivation or reduction to an acceptable level of all viable organisms which can be effected by moist or dry heat, gas (e.g. ethylene oxide), filtration and ionizing radiation (but not with ultraviolet radiation).

3. PERSONNEL

All personnel employed in pharmaceutical manufacturing areas should receive training in any areas relevant to the successful manufacture of drugs, including reference to hygiene and at least to the basic elements of microbiology. Initial training should be followed by suitable refresher courses in GMP.

3.1 Staff and Training

3.1.1 The organisational structure of the company shall be such that Production and Quality Control shall be headed by different persons, neither of whom shall be responsible to the other.

3.1.2 Each person responsible for supervising the manufacture of a drug product shall have the education, training and experience or any combination thereof, to perform assigned functions in such a manner as to provide assurance that the drug product has the intended quality.

3.1.3 In addition to the staff noted above, an adequate number of technically trained personnel should be available to carry out the production and control operations in accordance with established procedures and specifications.

3.2 Personal Hygiene

3.2.1 High standards of personal hygiene and cleanliness are essential.

3.2.2 Clothing has to be adapted to the process and to the working place in such a way that protection of the product and of the people from contamination is assured.

4. PREMISES

The premises must be located, designed of suitable designed, dimensions constructed, and equipped in such a manner that they will be suitable for the purposes of drug manufacturing. The individual working areas must be adequate so that any risk of confusion, cross-contamination, and other mistakes are reduced to a minimum.

4.1 In determining the suitability of premises regard should be paid to :

4.1.1 The compatibility of other manufacturing operations that may be carried out in the same or adjacent premises

4.1.2 The adequacy of the working space, which should allow orderly and logical placement of equipment and materials so as to :

- minimize the risk of mix-up between different drugs or their components
- control the possibility of cross-contamination by other drugs oor substances
- minimize the risk of omission of any manufacturing step

4.1.3 Those physical aspects of the premises that co ld affect the quality and safety of products :

buildings should be so designed and constructed as to prevent the entry of animals and insects; interior surface (walls, floors and ceilings) should be smooth and free from cracks and open joints, should not shed particulate matter, and should permit easy cleaning and if necessary disinfection.

4.2 All premises, including production areas, laboratories, stores, passage ways and external surrounding should be maintained in a clean and tidy condition.

4.3 Premises should be maintained in an adequate condition. The condition of buildings should be reviewed reguarly, and repairs effected where necessary. Special care should be excercised to ensure that building, repair of maintenance operations do not hazard products.

4.4 Lighting, ventilation and, if necessary, air conditioning are required to maintain a satisfactory environmental condition that will not adversely affect the drug product during manufacture and storage.

4.5 Drains should be of adequate size, and should have trapped gullies and proper ventilation. Any open channels should be shallow enough to facilitate cleaning.

4.6 The premises must comprise suitable and adequate changing rooms, wash rooms, and lavatory rooms,

4.7 Storage areas should provide adequate space, suitable lighting, and should be arranged and equipped to allow dry, clean and orderly placement or stored materials and products, whenever necessary under controlled conditions of temperature and humidity. Such areas should provide for suitable and effective separation of quarantined from other materials and products.

4.8 Sterile products must be processed in a specific area which is specially equipped and maintained to ensure cleanliness and sterility of the area.

4.9 Electrical power supply should be adequate to ensure the proper functioning of production equipment and laboratory instruments.

4.10 Extra precautions should be taken in dealing with Penicillin or other sensitising products to ensure that there is no cross-contamination of other products.

5. SANITATION

Manufacturing premises should be maintained in accordance with sanitary standards.

5.1 They should be clean, orderly and free from accumulated waste and free from vermin.

5.2 Unhygenic practices which should not be permitted in manufacturing areas include eating, drinking, smoking, keeping plants and storage of food and drinks.

5.3 Sufficient clean, well-ventilated toilet facilities including facilities for hand-washing and rooms for changing clothes, should be available near working areas for the use of manufacturing personnel.

5.4 Sinks should be excluded from aseptic areas. If installed in clean areas, they should be of suitable quality, without overflow, and be supplied with water of at least potable quality.

6. EQUIPMENT

6.1 Manufacturing equipment should be designed, constructed, placed and maintained in such a way :

6.1.1 to be suitable for its intended use

6.1.2 to facilitate thorough cleaning

6.1.3 to minimize any contamination, risk of confusion or the omission of a processing step during manufacturing.

6.1.4 to be located at a distance from other equipment sufficient to avoid congestion and to ensure that products do not become admixed or confused with one another.

6.1.5 that fixed pipework (and valves) should be clearly identified as to their contents.

6.2 Weighing and testing equipment used in manufacture, holding or quality control must be calibrated and checked at regular intervals and maintained properly to enable them to perform their proper functions.

6.3 Operating conditions within equipment used to sterilize drug products should be monitored.

6.4 Ultraviolet rays can only be relied upon to maintain sterility and not to achieve sterilization.

7. STARTING MATERIALS

A record should be made of all incoming starting materials. The record should contain information on the supplier, the origin (if possible), date of receipt, date of analysis, date of release and date of expiry (if any).

7.1 All such materials must be ;

7.1.1 properly identified & labelled, and their containers examined for damage

7.1.2 properly quarantined and stored

7.1.3 properly sampled by the quality control unit

7.1.4 tested for compliance with specifications (all materials should be marked to indicate that they are undergoing testing) ; and retest at certain intervals.

7.1.5 released from quarantine by the quality control unit by means of written instructions

7.1.6 issued for use only by an authorized person, following an approved and documented procedure. Stock records should be kept to indicate each receipt and issue so that stock reconciliations can be made.

7.1.7 dispensed by an authorized person following a defined procedure, to ensure that the correct materials are accurately weighed, measured or counted into clean, properly labelled containers. Each material and its weight, volume or quantity should be checked by an independent person and the check recorded.

7.2 Adequate areas, segregated from other activities, should be provided for weighing and measuring.

7.3 All rejected starting materials should be conspicuously identified, placed separately as such, and be destroyed or returned to the supplier as soon as possible.

8. PRODUCTION

The processes used in production should be capable of yielding, with the premises and equipment provided, finished products which conform to their specifications.

Defined manufacturing procedures are necessary to ensure that production, quality control and other relevant personnel are instructed in the details of the processes concerned.

8.1 Processing

8.1.1 Before the introduction of a Master Processing Procedures it should be evaluated sufficiently to determine that it is suitable for routine processing operations, and the ability of the process to give a reproducible and suitably homogeneous product should be validated

8.1.2 A similar evaluation should be conducted when any significant change in processing, equipment or materials occurs

8.1.3 Stability data on a product made in accordance with a new formulation, a significantly modified process, any change in packaging materials, or made from reworked material which might influence stability should be collected at an early stage

8.1.4 Processes and procedures should undergo a regular critical appraisal to ensure that they remain capable of achieving the intended results

8.1.5 Production staff should follow defined and authorised procedures for every stage of each manufacturing process

8.1.6 Any departures from defined procedures must be recorded and agreed upon with the Production manager and the person responsible for Quality Control before final release of the product

8.1.7 Before any manufacture begins steps should be taken to ensure that the work area and equipment are free from any materials, products, or documents, not required for the current operation

8.1.8 At all times during processing all materials, bulk containers and major itens of equipment used should be labelled or otherwise identified with an indication of the product or material being processed, its strength (where applicable) and batch number or control code. Where necessary such identification should also indicate the stage of production. The batch or lot number need not be identical with the code number used upon the label of the finished product but it must be related to it.

8.1.9 Before applying labels or marks to materials and equipment, all inappropriate or irrelevant labels or marks proviously used thereon should be removed or permanently defaced

8.1.10 The final yield, and any significant intermediate yield, of each production batch should be recorded and checked against the theoretical yield. In the event of a significant variation, steps should be taken to prevent release or further processing of the batch (or of any other associated batches or products processed concurrently, and with which it may have become admixed) until an adequate explanation can be found which does not prevent release or further processing

8.2 Packaging

A formally authorized Master Packaging Procedure should exist for each dosage form, package size and type of container

8.2.1 Packaging materials should be stored and handled in such a way as to ensure that those relating to different products do not become intermixed. Access to such materials should be restricted to authorized personnel

8.2.2 Prior to packaging and labelling of a given batch of a drug the Batch Processing Records specified should show that the batch has been duly tested and approved for packaging by the Quality Control unit

8.2.3 Prior to being issued, all labels for containers, cartons, boxes, inserts, leaflets, and other packaging materials, should be examined and released as satisfactory for use by the Quality Control unit

8.2.4 To prevent packaging and labelling errors a known number of labelling and packaging units should be issued and, if required, coded. Such issuance should be made against a written, signed request that indicated the quantity and types required

8.2.5 Upon completion of the packaging and labelling operations, a comparison should be made between the number of labeling and packaging units issued and the number of items labeled and packaged plus the number of units not used.

All coded unused units should be destroyed. Any significant or unusual discrepancy in the numbers must carefully be investigated

8.2.6 All finished drug products should be identified by labelling that should comply with government regulations

8.3 Cleanliness

Before any production operation is begun, a check should be made to ensure that all apparatus and equipment to be used in the operation has been cleaned and/or sterilized

8.4 Equipment and Containers

Equipment and containers being used in production and storage must be identified by conspicuously placed and clearly legible labels, bearing the name and/or identification code of the processed materials and the necessary batch identification data.

8.5 Recovered Materials

Material may be reworked, recovered or salvage by an appropriate and authorized method, provided that the material is suitable for such reprocessing, that the resultant product meets its specificarions and there are no significant changes in product quality ; stability tests should be conducted as necessary. Documentations should accurately record the reworking process carried out.

9. QUALITY CONTROL

Every manufacturing establishment should have a quality control system : so designed as to assure that drug products are manufactured in accordance with adequate conditions and procedures and will continue to meet the established specifications.
For this puppose there should be an appropriate and independent Quality Control unit

9.1 Quality Control is concerned with sampling, specifications. testing along with orgarization, documentation and release procedures which ensure that the necessary tests are in fact carried out, and that the materials are not released for use, nor products released for sale and supply until their quality has been judged to be satisfactory.

9.2 The Quality Control unit should have a laboratory adequately staffed and fully equipped for performing all quality control tests and analyoes, including any environmental control test, required before, during and after manufacture.

9.3 The Quality Control unit should have the following principle duties :

9.3.1 To establish and when necessary revise control procedures and specifications

9.3.2 To prepare detailed written instructions, for carrying out each test and analysis

9.3.3 To establish written sampling procedures and sampling plans

9.3.4 To retain samples for future reference

9.3.5 To pass or reject each batch of starting materials, intermediate products, bulk and finished products

9.3.6 To assemble and review all documentation relating to the processing, packaging and testing of each batch of finished product before authorizing release for sale

9.3.7 To evaluate the stability of all finished products (in an on going basis) ; starting materials and intermediate products where necessary, and to establish instructions for the storage of materials and products within the plant on the basis of appropriate stability data

9.3.8 To establish expiration dates and shelf life specifications on the basis of stability test related to storage conditions

9.3.9 To evaluate and approve any reprocessing or reworking procedures for products and materials

9.3.10 To recommend those suppliers of raw materials and packaging materials who are known or believed to be capable or reliably supplying products meeting the company's established quality standard.

9.3.11 To take part in periodic validation studies for those manufacturing processes which are likely to undergo significant change with time. Such changes may aries from significant variations in equipment, processing and materials.

9.3.12 To evaluate all complaints received or defects noted about any batch; if necessary in conjunction with other departments, and to take appropriate action.

9.3.13 To establish any reference substances specified in the current instructions for testing, and store these substances properly.

9.3.14 To maintain adequate analytical records concerning the examinations of all samples taken.

9.3.15 To examine returned drugs, to determine whether such drugs should be released, reprocessed or destroyed

9.3.16 To participate jointly with production in an active self-inspection program to comply with GMP requirements

9.3.17 Certain of the functions set out in sections 9.3.1., 9.3.2., 9.3.7. and 9.3.8.may be delegated to another relevant division of the company.

9.3.18 To recommend contract manufacturing operations which are capable of meeting the company's specified quality standard.

9.4 Outside Laboratory

Outside laboratories may be used to augment the quality control capabilities or capacity of the company laboratory, However, it is the manufacturer's responsibility that the outside laboratory meets all the criteria set forth in this general guidelines.

The quality of the final product remains the responsibility of manufacturer.

10. DOCUMENTATION

For manufacturing activities a documentation system must be prepared. A documentation system consists of instructions, descriptions, specifications and records which may or may not be batch related.

10.1 The system of documentation should be able to record the complete history of each batch of produced finished product, from starting material to the finished products.

10.2 It should also be able to record executed activities in maintenance, storage, quality control, distribution and other specific matter linked to the GMP

10.3 It should be adequate to permit investigation and tracing of defective products, to determine the utilisation and disposal of all starting materials, intermediate and bulk products and to allow investigation of manufacturing details and control system.

10.4 Documents should contain all necessary, but no superfluous data, to be kept up to date and any amendment should be formally authorised. It should include provision for periodic review and revision as necessary.

10.5 There should be system for preventing the use of any superceded document.

10.6 Where documents bear instructions they should be written in the imperative mood as numbered steps. They should be clear, precise manner, unambiguous and in language the user can understand. Such documents should be readily available to all concerned with carrying out the instructions.

10.7 The respective records and the reference samples of starting materials and finished products should be retained for a specified period of time.

10.8 The basic document in common use are :

10.8.1 Specification and Standards

10.8.1.1 Raw Material specification

10.8.1.2 Packaging Material specification

10.8.1.3 Intermediate, bulk and finished products specification

10.8.1.4 Assay and test methods (analytical, microbiological, etc.)

10.8.1.5 Expiration of raw materials

10.8.1.6 Expiration of finished product

10.8.2 Production

10.8.2.1 Master Production Document

10.8.2.2 Master Processing Procedure

10.8.2.3 Master Packaging Procedure

10.8.2.4 Batch Processing Record

10.8.2.5 Batch Packaging Record

10.8.3 Quality Control

10.8.3.1 Records of testing, assay, result, release or rejection of starting materials, intermediate, bulk and finished products

10.8.3.2 Standard Procedures for sampling and inspection

10.8.3.3 Certificate of analysis of raw materials and finished products

10.8.3.4 Record of stability test

10.8.4 Other supporting documents

10.8.4.1 Records of receipt, issue and balance of each starting material, intermediate, bulk and finished product

10.8.4.2 Operating procedures for specific equipment

10.8.4.3 Standard procedures and records for the maintenance and cleaning of equipment

10.8.4.4 Standard calibration procedures and records for specific instruments.

10.8.4.5 Standard procedures and records for the cleaning of manufacturing areas

10.8.4.6 Standard procedures and records for monitoring of air born particles and/or viable bacteria in specific areas

10.8.4.7 Standard procedure and records for pest control

10.8.4.8 Records of personnel training on GMP

10.8.4.9 Standard procedures for self-inspection

10.8.4.10 Standard procedures for product recalls

10.8.4.11 Standard procedures for handling of complaints, including adverse reaction reports.

10.8.4.12 Records of disposal or destruction of rejected materials.

10.8.4.13 Standard procedures for handling of returned goods

10.8.4.14 Distribution records

Several of above mentioned procedures, specifications and/or records may be combined together in one specific document.

11. SELF-INSPECTION

To maintain strict adherence to all manufacturing procedures and prescribed controls, it is advisable for a manufacturer to appoint a properly qualified team to conduct inspections of its overall production and control procedures. Written procedures describing the functions of the self-inspection program should be available and followed.

12. PRODUCT RECALLS

Responsibility and procedures for recall of drug products should be established by the manufacturer to facilitate the recall of a batch from any link of the distribution chain when this becomes necessary.

Any action taken to recall a product suspected or known to be defective or hazardous, should be prompt and in accordance with a pre-determined plan. The procedures to be followed should be specified in writing and made known to all who may be concerned.

13. DISTRIBUTION RECORDS

A complete and progressive recording system for the distribution of drug products should be readily available and easily followed. Information should be readily available to conduct a prompt, accurate and efficient drug recall whenever necessary.

14. COMPLAINTS AND REPORTS OF ADVERSE REACTIONS

Complaints regarding product quality or unexpected adverse reactions resulting from the use of a drug must be thoroughly investigated.

Reports of serious unexpected adverse reactions should be immediately forwarded to the appropriate authorities.

Written procedures describing the handling of all written and verbal complaints regarding a drug product should be established and followed.

Such procedures shall include provisions for review by the Quality Control unit. A written record of each complaint should be maintained in a file designated for drug product complaints.

15. RETURNED AND SALVAGED DRUG PRODUCTS

A manufacturer should establish procedures for holding, investigating and analysing returned drug products. Products may be returned because of complaints, damage, expiration, or other reasons which cast doubt on the safety, and quality of the drug products, and determining whether such products should be reprocessed or destroyed.

There should be separate procedures for evaluating salvaged products.

Procedures should be in writing and records must be maintained properly.

7. BPSの組織と人員

Republic of the Philippines
Department of Health
Office of Management Services
BIOLOGICALS PRODUCTION SERVICE
Alabang, Muntinlupa

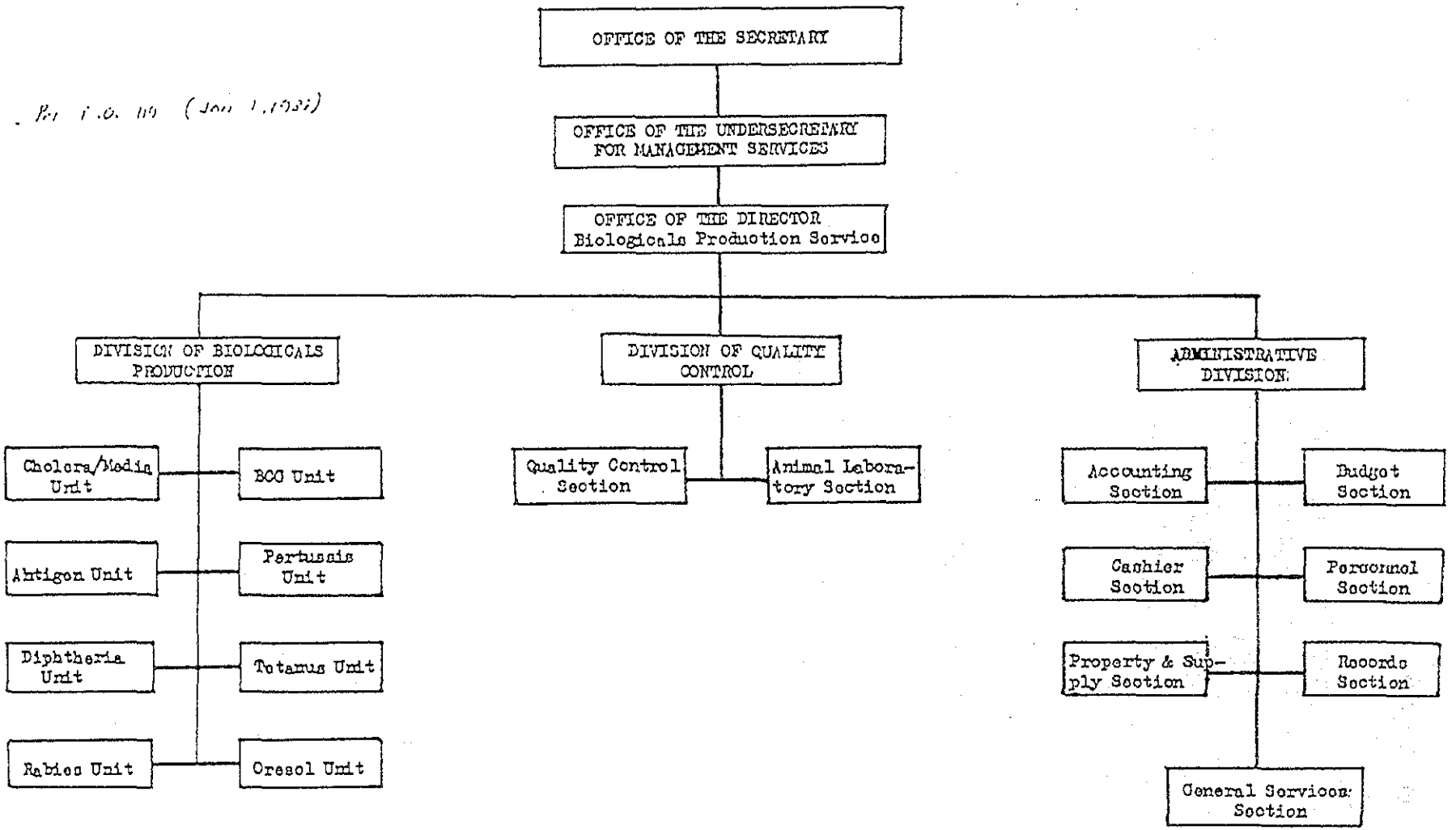
NUMBER OF POSITIONS IN THE BIOLOGICALS PRODUCTION SERVICE:

1989 - Filled up positions - 194
Unfilled positions - 16
TOTAL - - - 210

1988 - Filled up positions - 176
Unfilled positions - 34
TOTAL - - - 210

1987 - Filled up positions - 195

Per F.O. 119 (Jan 1, 1938)



Republic of the Philippines
Department of Health
Office of Management Services
BIOLOGICALS PRODUCTION SERVICE
Alabang, Muntinlupa

List of Professional and Educational Attainment of BPS Personnel
as of March 6, 1990

Office/Division	Male	Female	Total	Total No. of Personnel per Div.
Office of the Director				
Doctor of Medicine	1	-	1	
College Graduate	-	1	1	
College Level	-	1	1	3
Division of Biologics Production				
Pharmacist	-	6	6	
Chemist	-	1	1	
Medical Technologist	10	9	19	
College Graduate	2	17	19	
Vocational Graduate & College Level	13	13	26	
High School Graduate	26	12	38	
Elementary Level	13	-	13	122
Division of Quality Control				
Pharmacist	-	3	3	
Chemist	-	2	2	
Medical Technologist	-	2	2	
College Graduate	5	4	9	
Vocational Graduate & College Level	3	2	5	
High School Graduate	7	-	7	
Elementary Level	5	-	5	39
Administrative Division				
C P A	1	1	2	
Engineer	3	-	3	
College Graduate	5	6	11	
Vocational Graduate & College Level	9	3	12	
High School Graduate	2	1	3	
Elementary Level	3	-	3	34
		GRAND TOTAL		198

Republic of the Philippines
Department of Health
Office of Management Services
BIOLOGICALS PRODUCTION SERVICE
Alabang, Muntinlupa

1990~
Advice about
Future plan &
Request to Japan

The terms and reference of the BPS Advisory Committee are as follows:

1. To give advise on the formulation of manpower development program of BPS.

2. To help BPS identify the facilities and equipment required to improve vaccine production and other biological products including support services.

3. To recommend measures for improvement of vaccine production techniques.

4. To give advise in the formulation of effective and efficient system of filling, sealing, labelling, packing , storage and distribution of biological products.

5. To help improve the operational facilities and manpower of the Quality Control Division including the Laboratory Animals Section.

6. To help BPS plan for the expansion of biological production and quality control specifically to formulate an updated plan for the priority infrastructure facilities, equipment requirements taking into account the UNIDO Panel Recommendations, the Intercare Study of the Philippine proposal submitted to Japan.

7. To help BPS make plans for future BPS projects.

Composition of the Advisory Committee (BPS)

Dr. Norberto Ricacho
Dr. Antonio Jacalne
Ms. Eloisa Madrazo
Ms. Corazon Ramirez
Dr. Eulalia L. Venzon
Architect Augusto Consio

Republic of the Philippines
Department of Health
OFFICE OF THE SECRETARY

SAN LAZARO COMPOUND
RIZAL AVENUE, STA. CRUZ
MANILA, PHILIPPINES
TEL. NO. 711-50-80

October 12, 1988

DEPARTMENT ORDER
No. 295 s. 1988

S U B J E C T : Delegation of Authority to the Assistant Secretary in the Office for Standards and Regulations, Department of Health

Consistent with the provisions of A.O. No. 46, series 1988 placing under the administrative supervision and control of the Assistant Secretary in the OSR the Bureau of Food and Drugs, Biological Production Service, and the herbal processing plants in Regions II, VIII, XI and XII, the following administrative functions relative to these units are hereby delegated to the Assistant Secretary in OSR.

1. Approve original and promotional appointments and reinstatements to positions in the first and second level of the career service including supervisory positions below the level of the Chief of division (from range 38 to range 66).

2. Approve casual appointments.

3. Approve requests for permission to teach, exercise profession or engage in business outside office hours.

4. Approve leave applications including terminal leave of personnel.

5. Approve requests for temporary detail of employees from one of the above offices to another not exceeding 90 days.

6. Investigate administrative complaints against employees and recommend appropriate action to Secretary of Health through the Office of Assistant Secretary for Legal Affairs.

7. Approve requests for local travel not exceeding 30 days chargeable against the funds of the above mentioned offices.

CERTIFIED TRUE COPY
GREGORIA V. BAUTISTA
Chief, Records Section
Department of Health

8. Approve attendance of employees to conferences, seminars and non-degree training programs held locally, chargeable against the funds of the above mentioned offices.

9. Approve requests for authority to grant meal and transportation allowances for overtime services rendered, chargeable against the funds of the above mentioned offices.

10. Approve requisitions for service, supplies, materials and equipment subject to the approval of annual procurement plan.

11. Authorize the disbursement of funds and accordingly approve vouchers in payment of obligations for services rendered, as well as supplies, materials and equipment purchased.

The above delegation shall modify A.O. No. 40 s. 1988 accordingly.

This Order shall takes effect immediately.

ALFREDO R.A. BENGZON, M.D.
Secretary of Health

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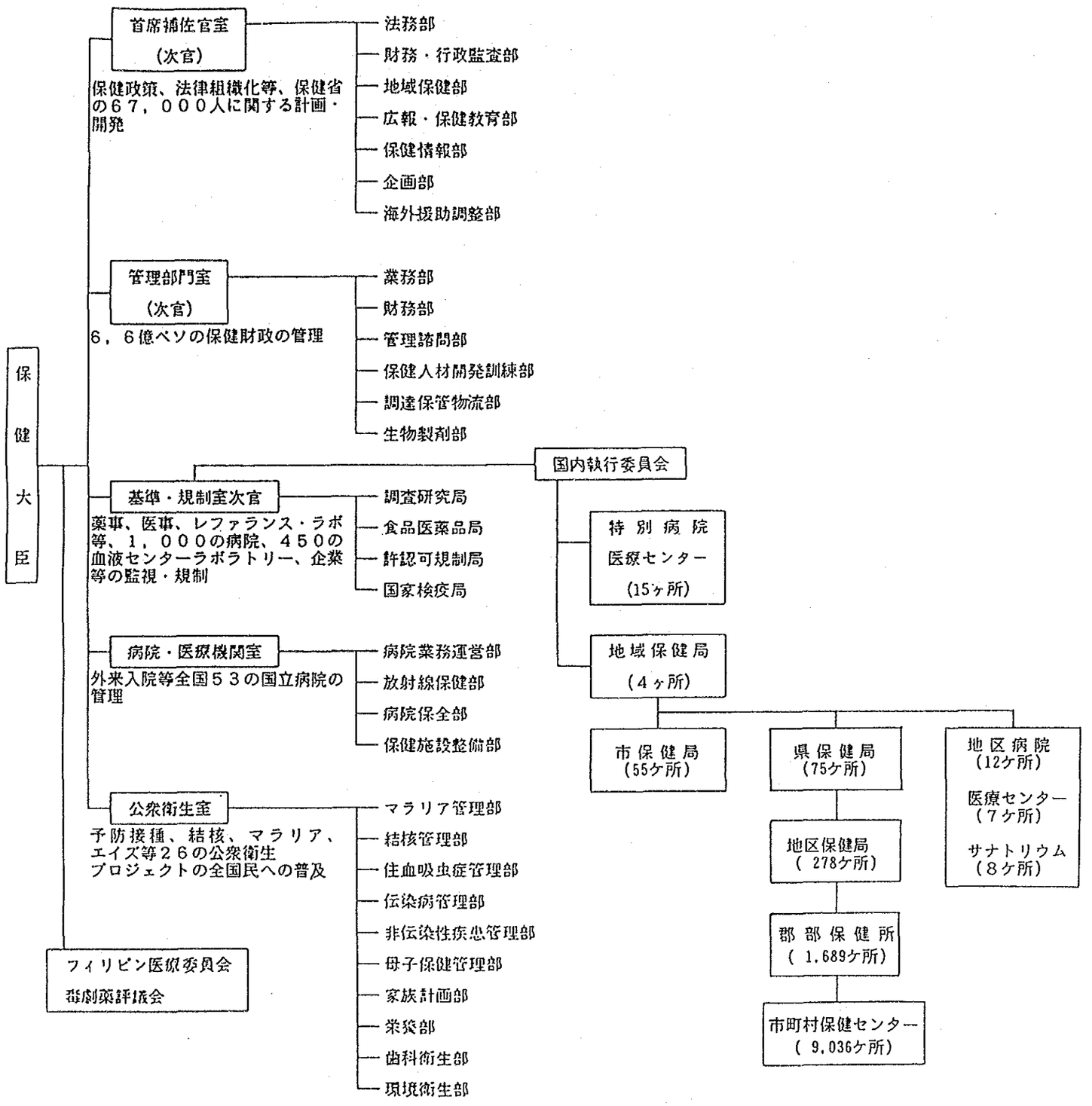
GREGORIA V. BAUTISTA
Chief Records Section
Dept.

8. 保健省組織図ならびに中期開発計画



DEPARTMENT OF HEALTH

Three Priority Areas of Action (Medium Term Development Plan 1988—1992)

1. Formulation and implementation of an efficient response to the main causes of morbidity and mortality (i.e., disease control and service delivery programs).
2. Provision of adequate attention and resources to the machinery that responds to health problems (i.e., the government health network and the network of private health care providers).
3. Establishment and maintenance of a climate conducive to health-oriented policies and programs (i.e., multi-sectoral action for health through advocacy, regulation and coordination).

Priority Area of Disease Control and Service Delivery

1. The five impact programs (EPI, Malaria Control, TB Control, Schistosomiasis Control and Diarrheal Disease Control) shall be sustained. Specific program weaknesses and deficiencies will be corrected. Implementation will be increasingly localized and decentralized consistent with the respective 5-year directional plans of these programs.
2. Services and programs oriented toward the health of mothers and children will be operationally integrated at the service delivery level. The concerns include reduced maternal morbidity and mortality, increased child survival and improved reproductive health among adolescents. Planning, program management and supervision, and monitoring will also be appropriately integrated at the various levels.
3. Appropriate support will be provided to the following programs: maternal, infant and child care; nutrition with a specific focus on mortality reduction, disability prevention and rehabilitation from malnutrition; dental health; family planning; environmental health; leprosy control; radiation health and safety; filariasis control and control of sexually-transmitted diseases.
4. In the medium-term, major program interventions will be launched and implemented in the following areas; acute respiratory illness control, cardiovascular disease control, cancer control and mental health. These are health problems of major proportions where programs are expected to be comparable in scale and scope to the five impact programs.

5. A focused program to prevent and control AIDS shall be established and expanded over the medium term. Based on present epidemiological outlook, AIDS could become a major public health problem within the next 5 years.

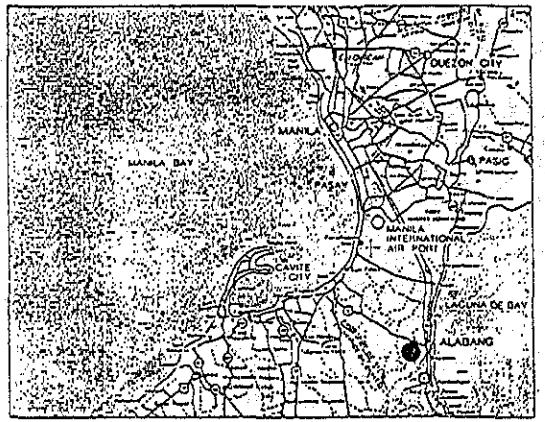
6. Medical care and hospital care services shall be expanded and improved. Access to professional care shall continue to be widened as household-based health practices are correspondingly improved. The barangay health station-rural health unit-district hospital system within a catchment area shall be established as the basic unit of integrated medical and hospital care delivery. Hospital networking as a mechanism for cross-referral and sharing of capabilities shall be done more extensively as well as intensively. Improvement of emergency room and out-patient facilities shall be given priority.
7. Private facilities, practitioners and non-government organizations (NGOs) in health shall be systematically involved in disease control and service delivery programs.
8. Programs shall be localized and integrated within a community-based framework. Appropriate technologies will be adopted to integrate basic national priorities and policies at the lowest viable level of community organization.
9. Health education programs will be implemented to raise public awareness and promote health-oriented behavior supportive of disease control and service delivery programs. A particular focus on anti-smoking, drug abuse prevention, breastfeeding, home management of diarrhea and acute respiratory illness, proper hygiene and sanitation, proper nutrition and other simple preventive and curative practice will be adopted.
10. Primary health care will be further advanced through the implementation of a program of community mobilization for health. The program has two broad measures: the mobilization of the formal health network to deliver basic health services to communities and the mobilization of organized communities in the health programs via decentralization, collaboration with local governments and joint action with NGOs for service delivery and health cause advocacy.
11. Basic support for disease control and service delivery programs shall be assured. Logistic support, training, monitoring, evaluation, research and development, and administrative and financial arrangements shall be improved. Resource constraints shall be considered in policy formulation and target setting. This will ensure that planning and budgeting will keep actual field conditions in mind. Central units shall be made more responsive and supportive to field service units.
12. Government performance in quarantine, licensing, regulation, food and drug administration and related regulatory activities shall be improved through more rational application of technical standards, systems streamlining, greater transparency and use of more cost-effective methods.

MISSION

The Research Institute for Tropical Medicine (RITM) is committed to pursue its Mission of conducting research in the field of infectious and tropical diseases that are of public health importance, with the overall Vision of reducing disease morbidity and mortality among the Filipino people.

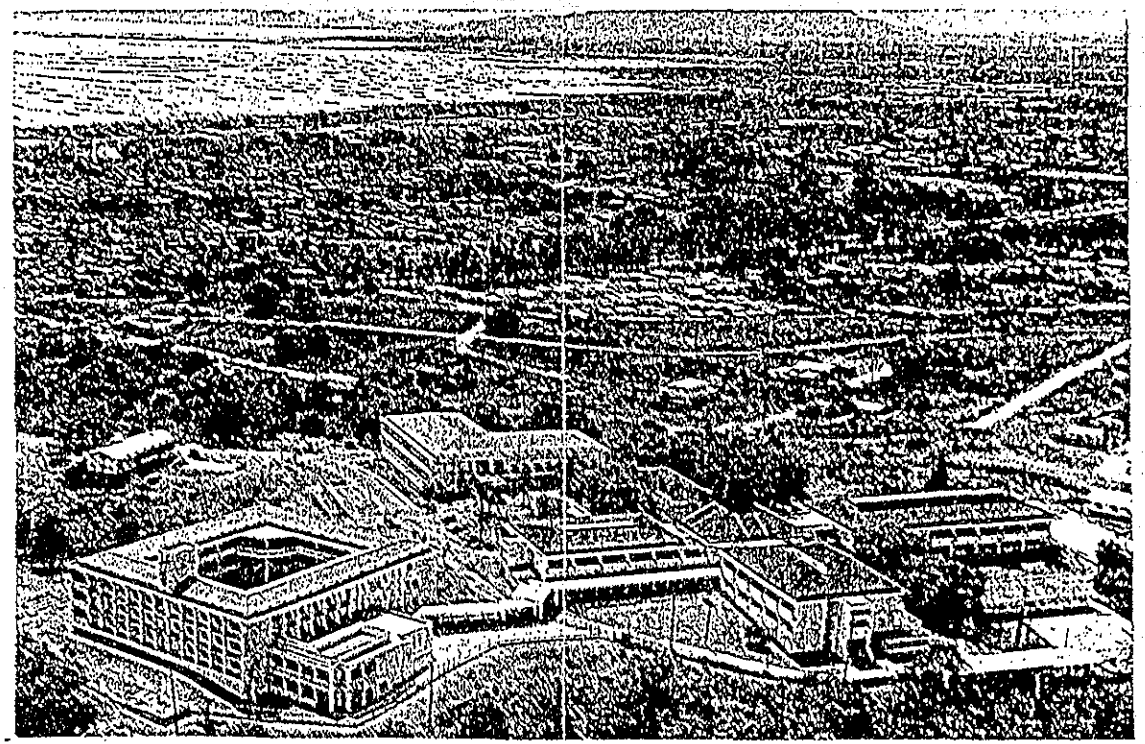
For further inquiries, please write to:

The Director
Research Institute for Tropical Medicine
Alabang, Muntinlupa
Metro Manila, Philippines
Tel. 842-28-28, 842-22-45
Telex No. 4213



RESEARCH INSTITUTE FOR TROPICAL MEDICINE

Department Of Health
Republic of the Philippines



BACKGROUND

The *Research Institute for Tropical Medicine* was established in 1981 by Executive Order No. 674 as a research facility under the Department of Health. The RITM is tasked with planning and implementing the Tropical Medicine Research Program in the Philippines.

MAJOR THRUSTS

I. Research

The primary function of RITM is to undertake research in the prevention, diagnosis and treatment of tropical diseases of public health importance. To be of utmost relevance to the National Health Plan, the research efforts of RITM are geared towards the development of new diagnostic techniques and the evaluation of effective and efficient intervention measures for the control of infectious tropical diseases. Its research findings are disseminated through local and international publications and forums and are submitted to health policy-making bodies.

II. Technology Transfer & Training

The RITM offers training programs in infectious diseases and research seminars for local health institutions. It also conducts laboratory training workshops for countries in the Asia-Pacific region. Technology transfer is also promoted through collaborative research with foreign institutions. Institutional manpower development is carried out by in-service and external training in laboratory and field research methods.

III. Health Services

Corollary to its research activities, the RITM participates in the delivery of health care through inpatient and outpatient services for infectious and tropical diseases. Its inpatient service consists of a 50-bed hospital, including an Intensive Care Unit. As a referral center for infectious diseases, the RITM provides these services in coordination with existing health care facilities in Muntinlupa and other

RESEARCH AGENDA & CAPABILITIES

The burden of illness and feasibility for control primarily define the research priority areas of RITM. Research projects are being carried out for the following infectious and tropical diseases: acute respiratory infections, amoebiasis and other intestinal parasitic diseases, dengue, diarrheal diseases, hepatitis B, HIV infections, leprosy, malaria, meningitis, rabies, schistosomiasis and vaccine-preventable diseases. Short-term investigations are also undertaken on special interest areas, such as tuberculosis diagnosis, legionellosis and sepsis neonatorum.

The design and facilities of the RITM are the most up-to-date for the conduct of valid and reliable investigations for infectious and tropical diseases. Among the various research technologies available are: monoclonal antibody technology, immunofluorescence microscopy, scanning and transmission electron microscopy, high-pressure liquid chromatography, virology examinations, production of antigens and antibodies for *S. japonicum* and hepatitis B virus, special techniques in the diagnosis of parasitic diseases, laboratory and field techniques for mosquito-borne diseases, breeding of experimental animals, HIV serology, rabies diagnosis in animals, rapid diagnostic techniques in microbiology, food microbiology and water bacteriology, and diarrheal disease microbiology and serology.

STAFF

The research staff of RITM include health and allied health personnel who specialize in health research management, laboratory methods of diagnosis and patient management. The areas of expertise and experience of the research staff include the disciplines of microbiology, virology, immunology, biotechnology, parasitology, electron microscopy, clinical management of infectious diseases, community medicine, epidemiology, biostatistics and health economics.

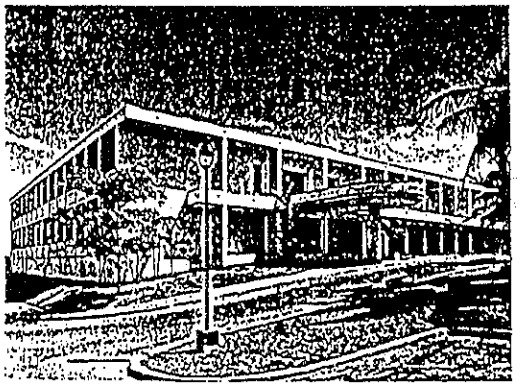
LINKAGES

The construction of RITM was made possible through a grant-in-aid provided by the Japanese government. A technical Cooperation Project was then implemented through the Japan International Cooperation Agency from 1980 to 1988.

Other local and international linkages have been established for research, training and service activities. Locally, these institutions include: the Muntinlupa Health Office, the University of the Philippines, hospitals of the Department of Health and a number of private hospitals from north to south. Linkages abroad include: Brown University (USA), University of Queensland (Australia) and the Academy of Finland.

Although RITM draws its appropriations from the national government, it also receives additional technical support and grants from the following: Philippine Council for Health Research and Development, Japan International Cooperation Agency, World Health Organization, Australian International Development Assistance Bureau, International Development Research Centre, International Atomic Energy Agency, Edna McConnel Clark Foundation, Ohyama Health Foundation, Rockefeller Foundation: Tropical Disease Research Joint Venture, Finnish International Development Agency, Helen Keller International and Family Health International.

As a research institution, RITM recognizes its responsibility as a center for the dissemination of the products of research. Activities for the promotion of effective transfer of technology and application of research outputs are thus areas afforded high priority by the scientists at RITM.

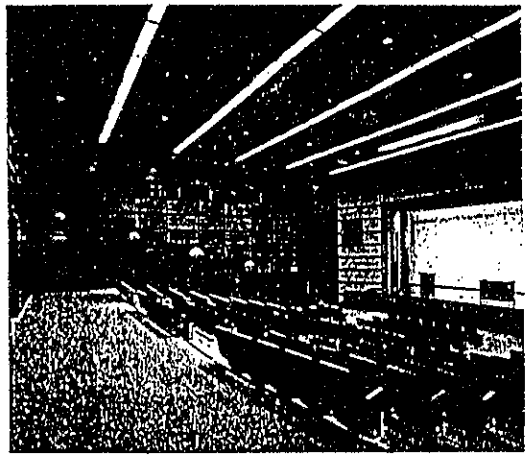


Training Center

THE CENTER FOR TRAINING IN TROPICAL INFECTIOUS DISEASES

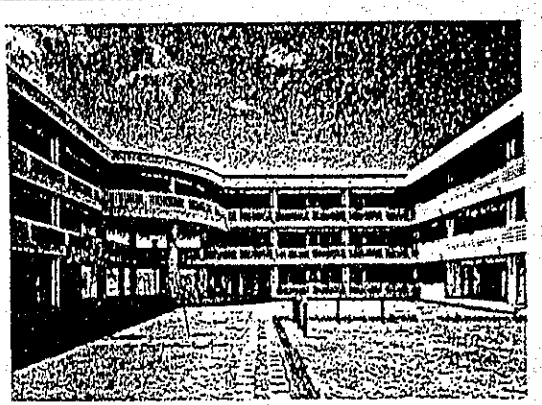
In 1989, through another grant-in-aid from the Government of Japan, The RITM Center for Training in Tropical Infectious Diseases was established for the expansion and integration of the RITM core facilities to include the training of medical and paramedical personnel from within the Institution, from other health agencies in the country and from other developing countries in the region. Through the Center for Training in Tropical Infectious Diseases, the benefits of research can be effectively disseminated in the Philippines and abroad.

audio-visual equipment such as slide projectors, overhead projectors, sound units, microphone units, projection screens and video units.



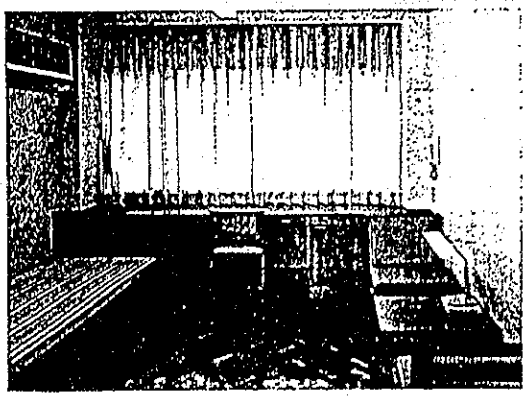
Conference Theater

Laboratories: The Training Center building has three laboratories with preparation rooms and clean bench rooms. Each laboratory can accommodate a maximum of 24 persons and has four 6-man experimental tables. The laboratories are equipped with basic equipment required for the conduct of research and training in bacteriology, virology, parasitology, biochemistry and tissue culture.



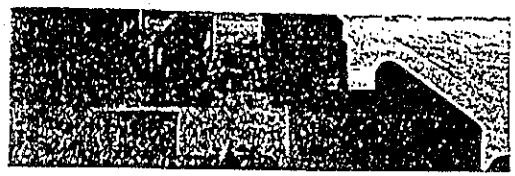
Residence Hall Courtyard

Faculty dormitory facilities include six individual occupancy rooms with airconditioning units and toilet and bath.



Airconditioned Faculty Room

Trainee dormitory facilities (participants' room) include 14 single rooms, 22 twin rooms (w/ T & B), 2 double-occupancy rooms and 2 quadruple-occupancy rooms (w/o T & B) for a total of 70 trainees.



Training Center Lounge

To promote exchange of ideas, biomedical technology and health training, the RITM conducts courses, workshops, seminars and symposia related to the tropical and infectious disease research programs being undertaken. It is also the aim of such training programs to establish a network between the RITM research scientists and health professionals, potential research workers and technicians from outside the Institution — both local and international.

Training activities for local health personnel and allied health workers, particularly those actively involved in the delivery of primary health care, are undertaken. Such activities are envisioned to bridge the gap in the nationwide efforts of control for infectious tropical diseases.

The RITM also works in close collaboration with health personnel from other developing countries throughout the region by establishing networks for the promotion of research and training activities.

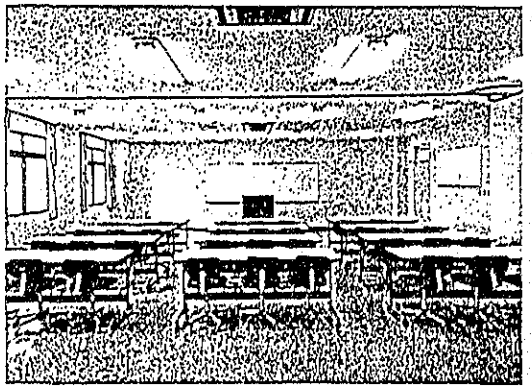
PHYSICAL FACILITIES

THE CENTER FOR TRAINING IN TROPICAL INFECTIOUS DISEASES

The Center for Training in Tropical Infectious Diseases is a two-storey building with the following facilities:

Conference theater. This facility is a 250-person capacity auditorium ideal for use in plenary sessions during seminars and con-

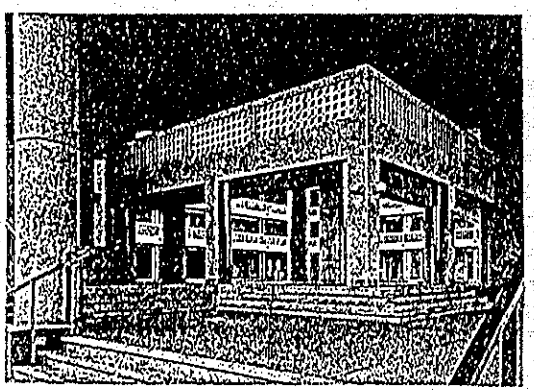
Lecture rooms. There are three lecture rooms, each of which can accommodate 30–40 persons. Provision for a larger lecture room with a capacity for 70 persons is possible.

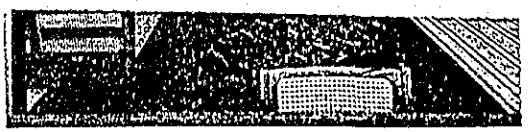


Lecture Rooms No. 2 & 3

RESIDENCE HALL BUILDING

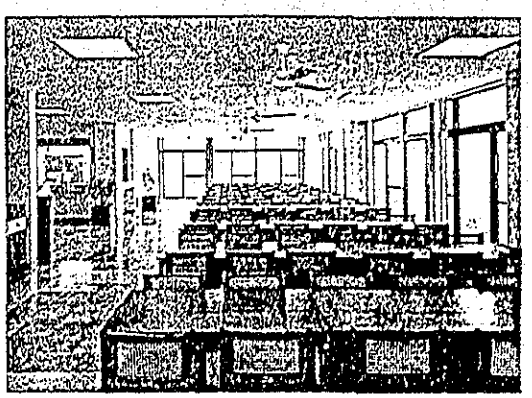
Dormitory facilities for course faculty, trainees and RITM staff are available. These are also open to private and other government organizations as venue for their activities like symposia, conferences, conventions, live-in seminars and workshops.



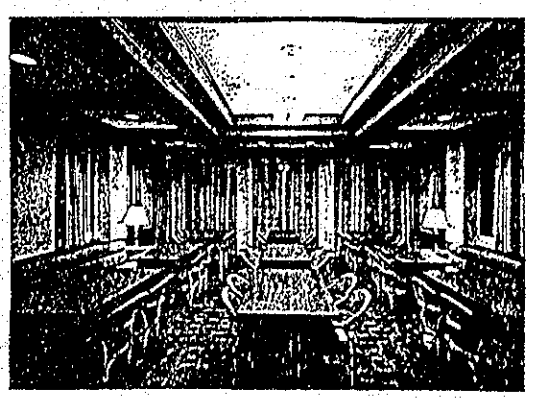


Participants' Room

The Residence Hall has a *dining hall* with a seating capacity of 110 persons. The *Executive Dining Lounge,* which is available for executive meetings and functions, can sit up to 40 persons. The RITM *Library* is also located at the top floor of the Residence Hall.



Dining Hall



Executive Dining Lounge

OUTLINE OF THE FACILITIES

Site Location	:	Alabang, Metro Manila
Total Floor Area	:	4,291 m²
Number of Storey	:	Two Storey
Construction Commencement	:	March 7, 1986
Construction Completion	:	March 15, 1987
Name of Buildings	:	Laboratory Building Energy Plant Building Water Tower Gas Storage Machine House Guard House
Max. Building Height	:	17.95 m (11.25m)
Principal Rooms	1F:	Audio Visual Room Offices Canteen Kitchen Storage
	2F:	Toxicology Lab. Food Micro-Biology Laboratory· Drug Micro-Biology Laboratory Clean Lab. Food Analysis Lab. Electro Microscope Room
Exterior Finish Roof	:	American Colonial Strip Shingle
Wall	:	Sprayed Exterior Paint
Interior Finish Floor	:	PVC tile, etc.
Wall	:	VP on Exposed Conc. VP on Cement Mortar
Ceiling	:	VP on Exposed Conc: Mineral Acoustical tile
Building Utilities	:	Air Conditioning Mechanical Ventilation Water Treatment & Supply Drainage, Gas Supply Sanitary Fixture Electrical Equipment

Purpose of the Project:

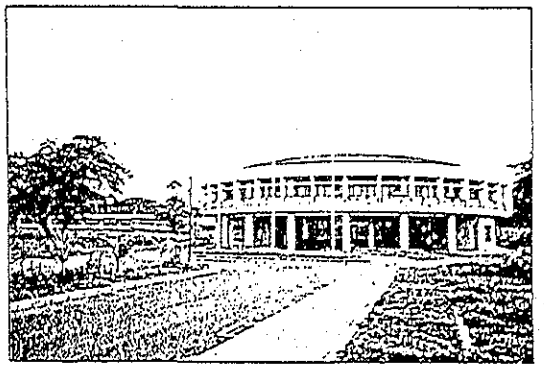
The purpose of the project is to assure the safety of food and drugs including traditional medicine household items, medical supplies, cosmetics and hazardous items, and supervise their production, sales and distribution in order to protect the people's health in the Republic of the Philippines.

Activities of food and Drug Laboratories:

1) Microbiolcgical tests.
2) Biological tests using test animals
3) Chemical analyses of food
   - on artificial additives
   - on hazardous natural substances
4) Physicochemical analysis of drugs
5) Inspection and Licensing
   - on facilities for food and drug
   - product evaluation

BUREAU OF FOOD AND DRUGS

Department of Health



JICA

Japan International Cooperation Agency

"FOOD AND DRUGS LABORATORIES PROJECT" by JICA
(Bureau of Food and Drugs, Department of Health)

BACKGROUND

It is a known accepted fact that the development in the field of health has been increasing at a much faster rate than the previous years. Medical breakthroughs are occurring at an increasing frequency together with tremendous progress in food and pharmaceutical industries. This has caused a need for the Bureau of Food and Drugs (BFAD) personnel to keep abreast with these latest developments.

The ASEAN countries have a joint collaborative program on pharmaceuticals and the Philippines is an active collaborating partner. The more notable points of ASEAN program which pertains to technical aspects are:

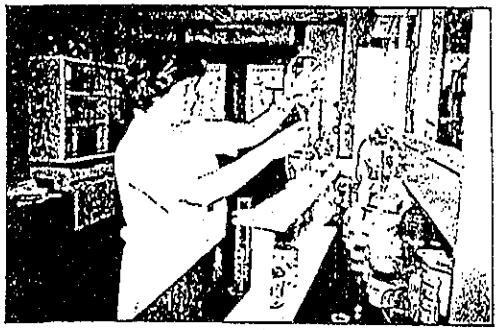
1. exchange of information on drugs;
2. training and exchange of expertise on drug supplies and management;
3. development, production and utilization of regional center and reference substances;
4. change of information on essential drugs list;
5. development of practical guidelines for the implementation of good manufacturing practices;
6. drug evaluation and control; and
7. development of adequate control labora-

Consistent with its charter and to make it more responsive in the light of changing conditions, there is a need to strengthen its capabilities and resources as a scientific regulatory agency including the Food and Drug safety control operation at the regional level to give full effect to its nationwide responsibility within the existing administrative framework.

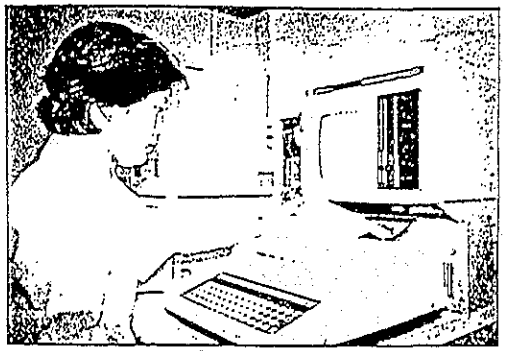
STRATEGIES

The strategies formulated by the Bureau of Food and Drugs are:

1. continuous training and exposure on new food and drug technology;
2. continuous training and seminars to be conducted by the beneficiaries of training for the different Food and Drug Regional Health Laboratories personnel;
3. documentation and dissemination of acquired information and materials;



4. periodic review and revision of standard operating procedures of product evaluation;
5. periodic review and revision of literature on the developments of foods, drugs and other products while in the local and international markets;
6. strict monitoring of product literature and advertisements; and



PROJECT DESCRIPTION

This project involves the construction of the building of BFAD, installation of appropriate equipments for laboratory works, the training of the personnel of the BFAD in Japan and dispatch of Japanese experts to the Philippines.

1. Grant-Aid (JICA)
   Term: FY 1985-FY1986
   Total budget: ¥ 1.497 billion
2. Technical Cooperation (JICA)
   Scheduled term: August 1986-July 1991
   JICA Experts dispatched from Japan:
   Atsuo UJIIE, M.D. (Team Leader, Microbiologist)
   Atsushi TASAKA (Project Coordinator)
   Masatsugu NAKASO, D.V.M. (Veterinarian)
   Toshiaki NISHIGAKI, M.D., Ph.D. (Pathologist)
   Takako MIURA, Ph. D. (Pharmacist)

Philippine counterpart training in Japan

Animal Care and Control	1987
Bioassay	1987
Mycology and Electron Microscopy	1987
Antibiotics	1988
Pesticides	1987
Food and Additives	1987
Pesticides	1989
Instrumental Analysis of Drugs and Preparation of Reference Standards	1989
Inspection of Import &	

Inspection & Evaluation of Drugs	1988
Plant Operation	1988

SUPPORTING ORGANIZATIONS IN JAPAN

- Bureau of Environmental Health and Bureau of Pharmaceutical Affairs, Ministry of Health and Welfare, Japan
- National Institute of Hygienic Sciences
- Food and Drug Safety Center, Inc. Hatano Research Institute
- Pharmaceutical Affairs Division Department of Environment and Public Health. Osaka Prefectural Government

How to Avail of Services:

Contact BFAD Office in Alabang or the Regional Offices of the Department of Health.

Contact Persons for Regional Health Offices:

Region I — San Fernando, La Union
— Dr. Conrado K. Galsim, Jr.
Regional Health Director

Region II — Tuguegarao, Cagayan
— Dr. Sulpicio P. Legaspi
Regional Health Director

Region III — San Fernando, Pampanga
— Dr. Aurora Villarosa
Regional Health Director

Region IV — Quirino Labor Hospital, Quezon City
— Dr. Edilberto G. Fernando
— Regional Health Director

Region V — Legaspi City
— Dr. Manuel N. Lorenzo
Regional Health Director

National Capital Region — Manila
— Dr. Carmencita Rheodica
Regional Health Director

Region VI — Iloilo City
— Dr. Prudencio J. Ortiz
Regional Health Director

Region VII — Cebu City
— Dr. Felicito F. Aniceto
Regional Health Director

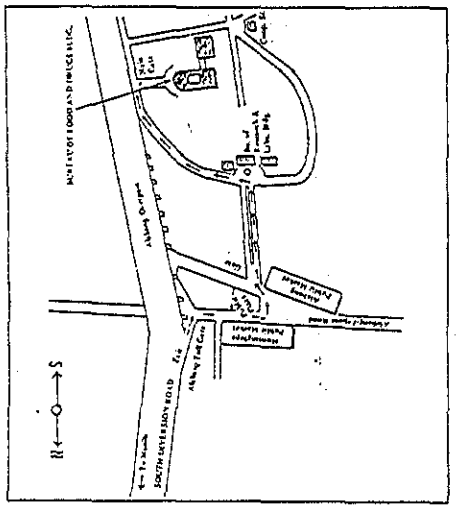
Region VIII — Tacloban City
— Dr. Luis D. Montero
Regional Health Director

Region IX — Zamboanga City
— Dr. Milagros L. Fernandez
Regional Health Director

Region X — Cagayan de Oro City
— Dr. Candido Tan
Regional Health Director

Region XI — Davao City
— Dr. Alfredo S. Mercado
Regional Health Director

Region XII — Cotabato City
— Dr. Eduardo L. Mariano
Regional Health Director

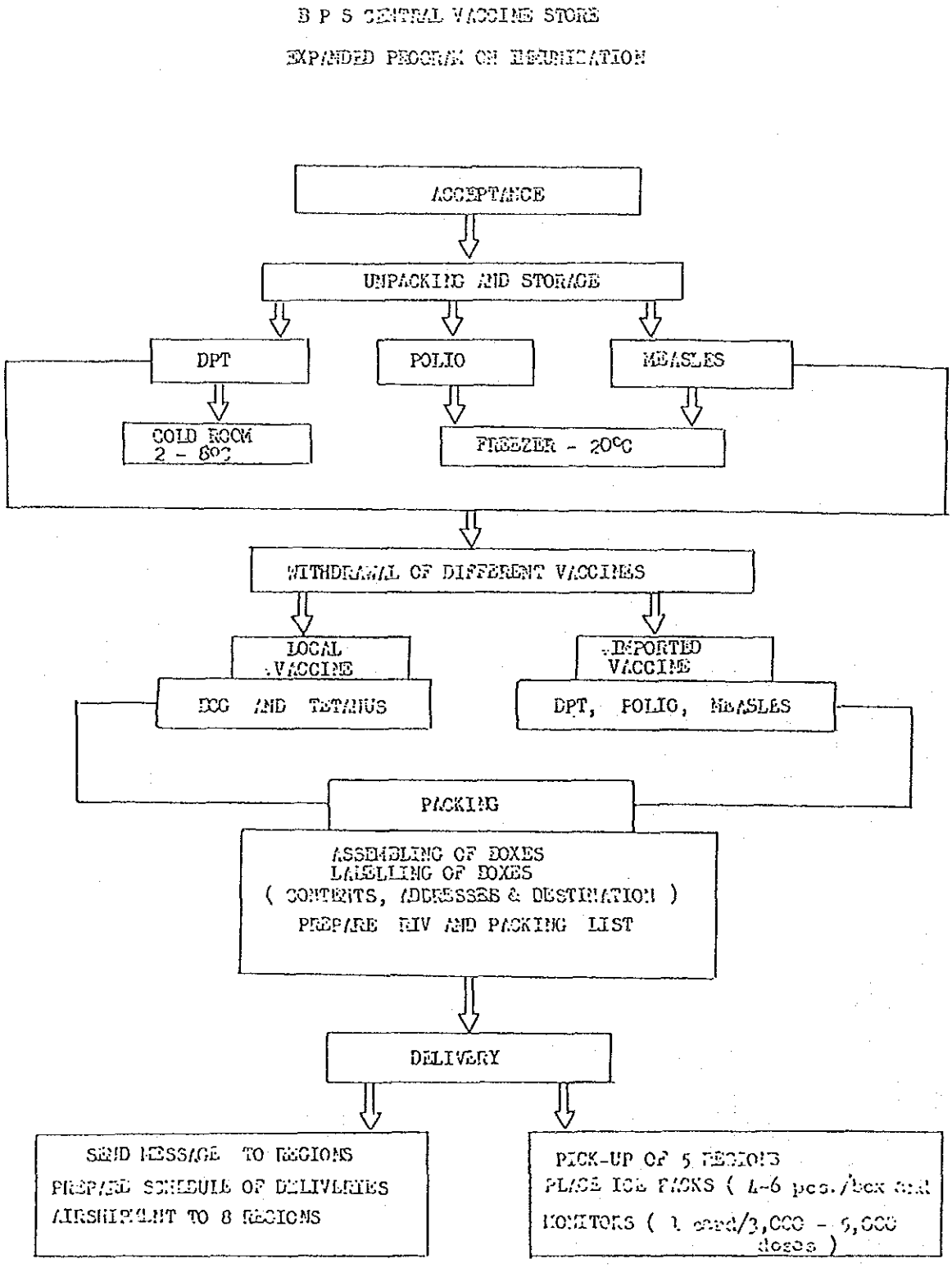


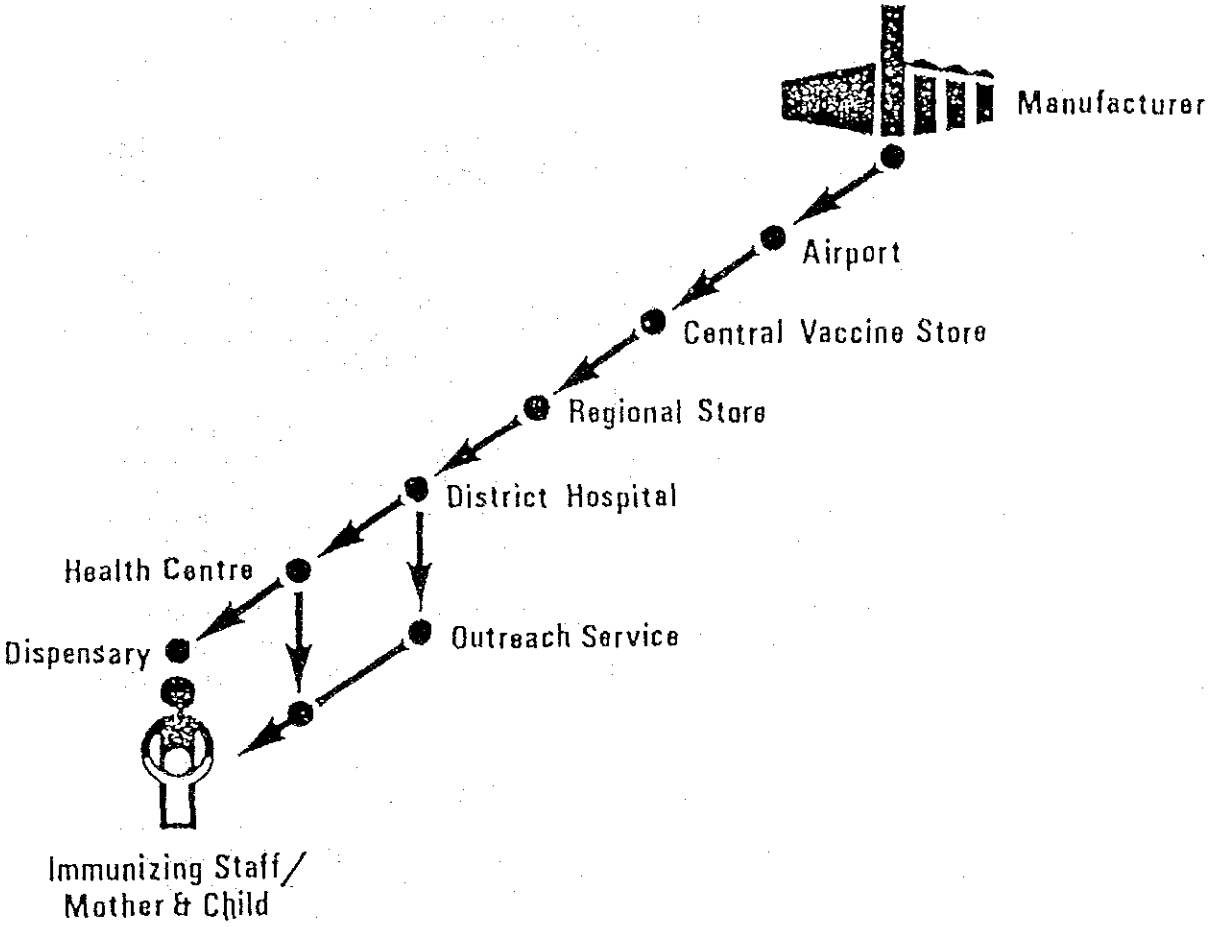
JICA

JICA Philippine Office
12th Floor, Pacific Star Building
Senator Gil J. Puyat Avenue Ext.
Cor. Makati, Ave, Mkt., M.M.
Tel. No. 88-30-81

Bureau of Food & Drugs
DOH Compound Alabang
Muntinlupa, Metro Manila
Philippines
Tels.: 842-22-05; 842-56-35
Loc. 231

11. フィリピン・コールドチェーン組織の資料




Manufacturer
Airport
Central Vaccine Store
Regional Store
District Hospital
Health Centre
Dispensary
Outreach Service
Immunizing Staff/
Mother & Child

Guidelines on the Distribution of EPI Vaccines
to Regional Health Offices

Biologicals Production Service is responsible for the shipment of vaccines to Regional Health Offices or selected cities or provinces with the following guidelines:

1. EPI vaccines shall be shipped on a quarterly basis. Emergency shipments maybe made on a case to case basis depending on justification and proper endorsement of the Maternal and Child Health Service.

2. The sending agency shall notify the recepients of vaccines about the arrival of vaccine at least ten days before the expected date of arrival. One or two days prior to shipment a telegram shall be sent indicating date and time of arrival of vaccines.

3. Sending agency shall ship vaccines to destinations within three hours of dispatch. No shipment of vaccine shall be allowed to stay at the domestic airport longer than 5 hours.

4. To minimize problems on communication; no shipment shall be made on Monday and Friday.

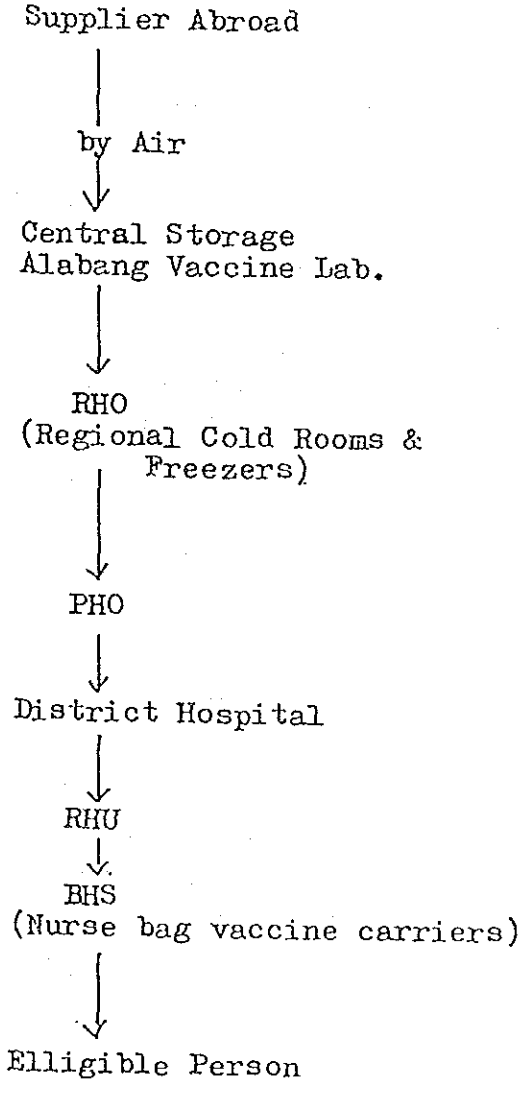
5. For Luzon Regions (Region 1-IV and NCR) shipment shall be made by land unless otherwise specified.

6. Regions V - XII (Bicol, Visayas and Mindanao region)- vaccine shall be sent directly to the regions by plane for storage in the regional cold room. Shipment maybe made direct to provinces or cities where there are airport facilities upon requests and endorsement of corresponding regions.

THE COLD CHAIN

The Cold Chain is a system for ensuring the potency of a vaccine from the time of manufacture to the time it is given to a child or a pregnant woman. The Cold Chain has two essential elements: people and equipment. People organize and manage the distribution of vaccines using equipment to store and transport the vaccines. All levels of EPI managers and implementors are involved in the cold chain, and equipment includes vaccine production facilities at the national and international level, down to transport boxes used to carry vaccines to outreach sites.

DIAGRAM 4-1: VACCINE DISTRIBUTION SCHEME



An effective cold chain is vital to the immunization program. Vaccines will confer immunity only when they are potent and to be potent they must be properly stored, handled and transported. The following table shows the recommended storage temperature for each vaccine. Vaccines are listed in order of their sensitivity to heat, with the most sensitive first.

Recommended Storage Temperature
of EPI Vaccines

	TYPE OF VACCINE	STORAGE TEMP.
MOST SENSITIVE TO HEAT	Oral Polio	-15°C to -25°C
	Measles (freeze dried)	-15°C to -25°C
	DPT	2°C to 8°C
LEAST SENSITIVE TO HEAT	BCG(freeze dried)	2°C to 8°C
	Tetanus Toxoid	2°C to 8°C

THE COLD CHAIN MANAGER

The person directly responsible for cold chain management at each level is called the Cold Chain Manager. The duties of the Cold Chain Manager are outlined in Chapter I.

DISTRIBUTION OF VACCINES

The following steps should be taken to ensure that vaccines are properly collected and transported.

a. Obtain the right amount of vaccines needed by preparing an inventory report and calculating your vaccine requirements for a specific period,
b. Make sure that you have enough storage facilities for your collected vaccines.
c. Check types and amounts of vaccine, diluents and ice packs.

d. Check the expiry date of the vaccines. Do not accept expired vaccines.

e. Put fully frozen ice packs or cold packs around the sides and bottom of the transport box.

DPT and TT are damaged by freezing. See to it that these vaccines will not be frozen in the cold box. Place frozen ice packs on table for five to ten minutes before packing so that the temperature of the ice packs will not be lower than $0^{o}C$.

f. Pack the vaccines and diluent into the cold chain container quickly and properly.

Transport boxes should be used to transport vaccines from the Regional to Provincial to District levels and then to Main Health Centers. From Main Health Centers to barangays, vaccine carriers may be used when there are only a few ampules/vials of vaccines.

g. Take the shortest route to your destination.

h. Transfer vaccines and diluent immediately to cold chain facilities (refrigerators/freezers/ cold room). In case there are no refrigerators or freezers; then transport box may be used for temporary storage for not more than five days.

If vaccines are shipped by air or sea, personnel receiving the vaccines should be notified as to the date and time of arrival.

Upon arrival, confirmation of the number of vaccines and diluents, along with the transport temperature should be provided to the sending office.

TEMPERATURE MONITORING

Monitoring Temperatures of Cold Rooms, Refrigerators, and Freezers:

The temperature of cold rooms, refrigerators, and freezers must be monitored once during the first working hour of the morning and again during the last working hour in the afternoon. Temperatures should be recorded on the Temperature Monitoring Chart.

Monitoring Temperatures with a Cold Chain Monitor:

Cold Chain Monitors are cards used to monitor the temperature of vaccines during distribution or visits to the field. They are only effective when:

- The spaces for date in, index and location are properly filled up as soon as vaccines are received.
- Breaks in the cold chain indicated by the windows of the monitor are reported immediately to the next higher level as soon as they are detected.

How to Use a Cold Chain Monitor Card:

a. Upon arrival of vaccines, check the vaccine cold chain monitor and fill up the columns for date in, index, and location.

b. If all the windows A, B, C, and D are white, the vaccines have never been exposed to temperatures above +10°C.

c. If window A is half blue, vaccines have been exposed to temperatures above +10°C; and the vaccines have been slightly damaged. However, all vaccines can still be used for immunization.

d. If window A turns all blue, vaccines have been exposed to temperatures of at least 12°C for two days. Polio vaccine should not be used. All other vaccines should be used.

e. If windows A and B are all blue; vaccines have been exposed to 12°C for eight days or 21°C for four days. Polio vaccines should not be used. Measles vaccines should be used within three months. Other vaccines should be used normally.

f. If windows A to C are completely blue and D is white, vaccines have been exposed to temperatures above 12°C for 14 days or 11 days at 21°C. Polio and measles vaccines should not be used. DPT and BCG should be used within three months. Tetanus Toxoid can be used normally.

g. If only D is blue; there has been a break in the cold chain and the vaccines have been exposed to temperatures higher than 34°C. for at least two hours. Check the cold chain. Vaccines can be used normally.

h. If windows A,B,C and D are all blue, vaccines should not be used.

VACCINE COLD CHAIN MONITOR

Date in	Index	Location	Date out	Index

INDEX/INDICE/

MONITOR U.S. Pat. C. MARK No 3,037,611	A	B	C	D D D D D
	If A all blue	If B all blue	If C all blue	If A,B,C & D all blue
POLIO	Test vaccine before use			
MEASLES		Use w/in 3 months		
DPT & BCG	These vaccines may be used		Use w/in 3 months	
TT &DT				

SUPPLIER	Name:
	Nom: _____
	Date of Dispatch: _____
	Date of Expedition:
FOURNISSEUR	Vaccine: _____
	Vaccin:

MAINTAINING COLD CHAIN EQUIPMENT:

Care of refrigerators and freezers:

If you have more than one refrigerators or freezer, put them all in room (the cold room), and observe the following points:

- Ensure that the room is well ventilated and protected from outside light and heat.
- Place refrigerators about 10 cm. away from the wall to allow movement of warm air.
- Ensure that each piece of equipment is permanently connected to the electrical supply.
- Keep doors and lids firmly shut.
- Defrost and clean refrigerators regularly.
- Place bottles of water in the refrigerator to help maintain storage temperature.
- Do not place food items in the refrigerator.

Transport boxes and vaccine carriers:

After each use:

a. Clean boxes/carriers thoroughly and leave lids open to allow for complete drying.

b. Examine all surfaces and repair cracks immediately.

During and between use:

- Keep boxes and carriers away from direct sunlight.

Equipment Inventory:

The EPI Nurse Coordinator should conduct a semi-annual inventory of cold chain equipment at the next lower level. A copy of the inventory report should be submitted to the next higher level.

Equipment Monitoring:

A trained technician should make regular visits to health facilities with cold chain equipment to ensure that refrigerators and freezers are in good condition. Visits should be conducted at least semi-annually.

Storage of VACCINES

With accurate planning and effective distribution, vaccine should not need to be stored for long period of time at each level. The maximum duration of storage should not exceed:

At the REGIONAL level:	6 months
At the PROVINCIAL level:	3 months
At the DISTRICT level:	3 months
At MAIN HEALTH CENTERS (with refrigerators)	1 month
At MAIN HEALTH CENTERS (using transport boxes)	not more than 5 days

Order of Vaccine Use:

Stored vaccines should be arranged according to type, expiry date, duration of storage and number of times they have been brought out to the field.

- Vaccines that have been stored the longest should be distributed or used first.
- Vaccines that will expire first should be distributed or used first.
- Ampules/vials of vaccines should be marked with an X each time they are carried to the field.

  X indicates one trip to the field . . .

  XX indicates two trips to the field . . .

  If vaccines are not used on their third trip to the field, they should be discarded.

HANDLING OPENED OR RECONSTITUTED VACCINES

Opened or reconstituted vaccines should be placed in a cup of ice or in a special cold pack during immunization sessions.

Opened or reconstituted vaccines should be discarded properly.

After four hours . .. discard BCG.
At the end of the working day . . . discard DTP, Polio, Measles & Tet.Toxoid.

Discarding Vaccines:

- Pour vaccines from opened vials into the group or into the latrine.
- Destroy or break empty vials.

THE REGIONAL COLD ROOM MANAGER

The Regional Cold Room Manager is designated by the Regional Director and trained by the Regional Immunization Officer or Nurse Coordinator. The duties of the cold room manager are to:

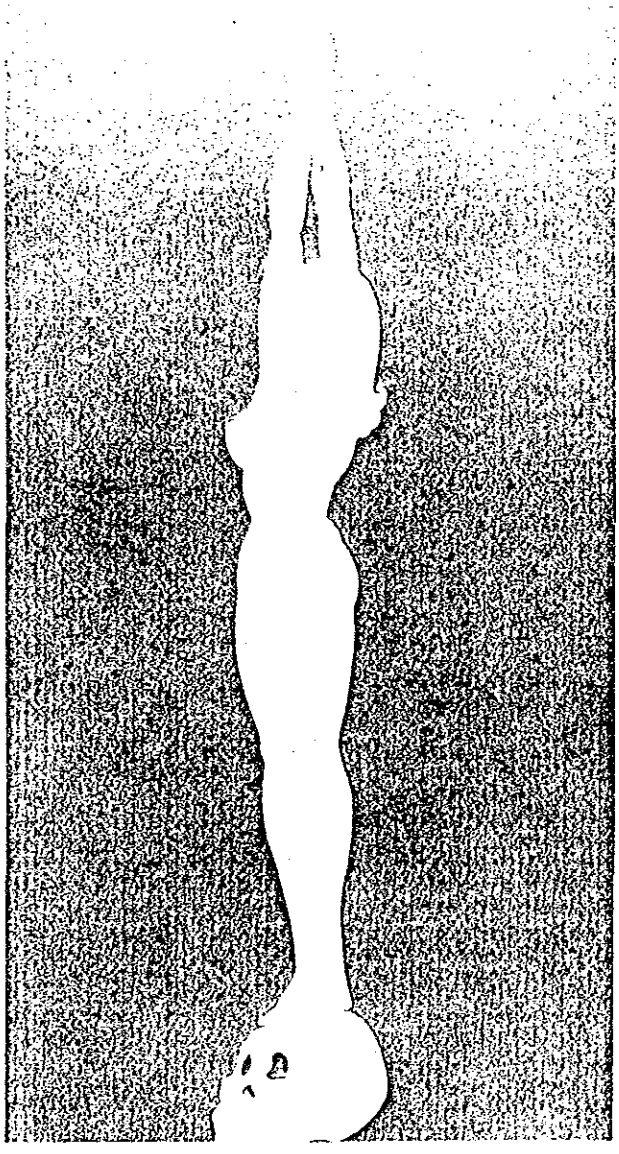
a. collect, store and distribute vaccines.
b. monitor the temperature of vaccines once during the first working hour of the morning and then again during the last working hour in the afternoon. The temperatures should be recorded on the temperature monitoring chart.
c. check and fill up the cold chain monitors.
d. update vaccine control record.
e. prepare a monthly inventory of vaccines.
f. maintain cold chain equipment.
g. prepare a monthly inventory of cold chain supplies and equipment and submits inventory report to EPI Nurse Coordinator.
h. report immediately to a traines technician for any breakdown or brown-out in cold chain facilities.
i. implement emergency plan in case of breakdown or brown-out.

IV. DOG LABORATORY

QUANTITY	EQUIPMENT	ORIGIN
5	Laminaire Flow Hoods	U S A
1	Vacuum Freeze	U S A
1	Water Bath	
2	Refrigerator	
1	Inspissator	
2	Incubator	U S A
1	Spectrophotometer	U S A
1	Warburge Apparatus	Germany
1	Autoclave	U S A
1	Automatic ampule filler and sealer	U S A
1	Analytical Balance	Switzerland
1	Distilling Apparatus	U S A
6	Filtration Apparatus	Denmark
	Ampule Sealing Machine	Japan

ANNUAL REPORT 1988

BIOLOGICALS PRODUCTION SERVICE



BIOLOGICALS PRODUCTION SERVICE
ALABANG, MUNTINLUPA
PHILIPPINES

CONTENTS

One of the significant aftermaths of the EDSA Revolution was the major reorganization of the government bureaucracy. The signing of Executive Order No. 119, otherwise known as the Reorganization of the Department of Health (DOH), resulted in the separation of the Division of Biologicals from the Bureau of Research and Laboratories. The separated division was revitalized and became a major Support Service Unit, now known as Biologicals Production Service (BPS). With the enunciation of the Philippine National Drug Policy by President Corazon C. Aquino in 1987, the BPS assumed a crucial role as one of the principal government units on which the third pillar of the National Drug Policy, self-reliance in pharmaceutical products, is anchored.

MESSAGES

Our country's National Drug Policy (NDP) challenges the Department of Health to be responsive to the physical, as well as socio-economic well-being of the Filipino. The crafting and implementation of this landmark policy takes place during a period of crisis in which the nation still quivers in the throes of change *associated with the arduous construction* of a free and democratic society.

The freedom we have won and defended would never have meaning unless our people are free from the shackles of sickness. It is therefore incumbent on government, as servants of the people, to take all possible measures to deliver them from the threats of infectious diseases. The BPS has been tasked with meeting these challenges, and serve to as a firm underpinning of the Self-Sufficiency pillar of the NDP that is aimed at reducing our dependence on transnational companies.

Through the BPS, the Filipino people can make headway in the entire world's *drive towards health for all by the end of* the millenium.

Dr. Alfredo Bengzon
Secretary
Department of Health

The Biologicals Production Service of the Department of Health has been revitalized to fulfill a pivotal and urgent role in its fight against the deadly communicable infectious diseases which stalk millions of Filipino children.

It helps the Philippines attain the objective of self-reliance in strategic pharmaceuticals by providing locally-processed and manufactured vaccines readily available to the people.

Dr. Quintin Kintanar
Assistant Secretary
for Standards and Regulation

Biologicals Production Service assumed its expanded role with firm resolve. Inspired by bold, earnest, and firm leadership, the BPS is privileged, rather than daunted, by its multi-faceted tasks.

History bears that BPS has always responded to the needs of the times. It was in fact, created in 1806 (as the Central Board of Vaccination) to combat smallpox, the spectre that threatened the population of the young republic.

Today, as the nation enters an era of virtual rebuilding, BPS has been reorganized to help look after the state's future citizens.

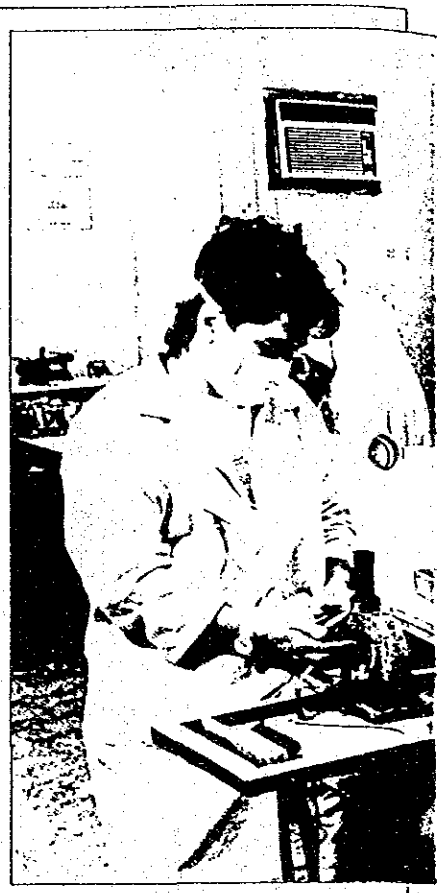
I am positive that, with the new impetus given to the dedicated men of BPS, the office will again live up to expectations.

Dr. Bernardo Mora
Director
Biologicals Production Service

STATEMENT OF MISSION

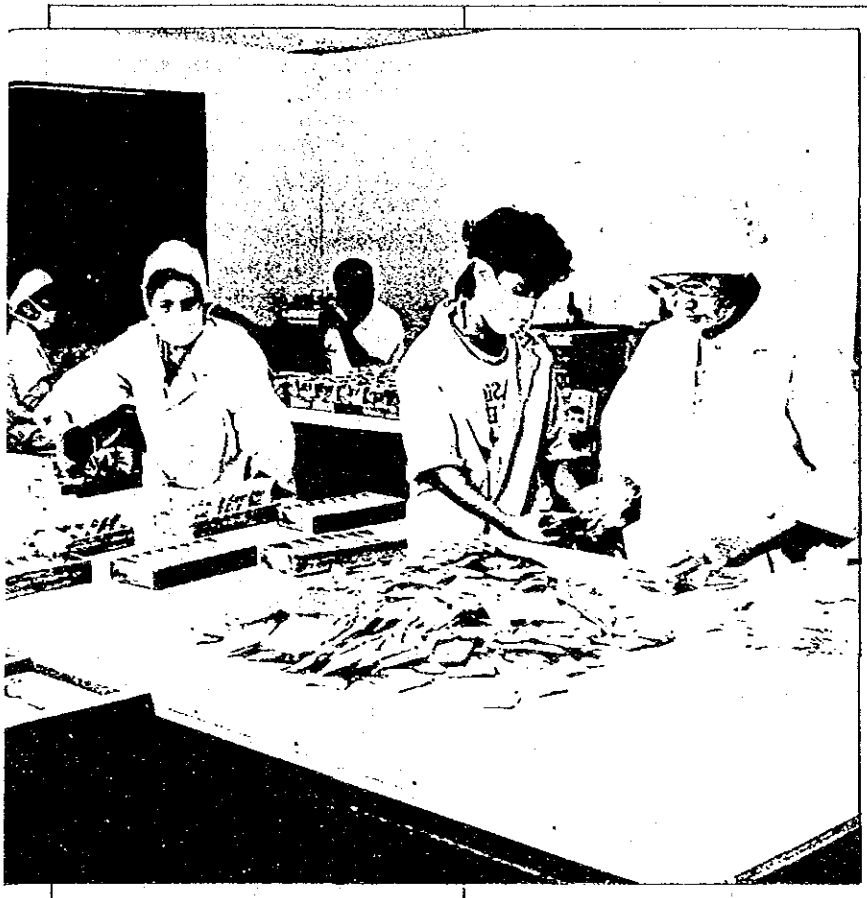
The Biologicals Production Service (BPS) is mandated under E.O. No. 119 to formulate plans, policies, programs, standards, and techniques for the processing, manufacture, standardization, and improvement of biological products for the use of the Department of Health; manufacture vaccines, sera, antitoxins, and other biologicals; provide consultation, training, and advisory services to implementing agencies; and conduct studies and research related to biologicals production, distribution, and use.

Its mission and mandate is crucial because up to the present, immunization through the use of vaccines is the most cost effective way of controlling communicable diseases which is the number one public health problem of the country.



In line with this mandate, the BPS is tasked to support two major programs of the DOH, namely:

- The expanded Program of Immunization (EPI) through the manufacture of quality EPI vaccines (BCG, Tetanus Toxoid, Oral Polio, DPT, and Measles) and the distribution of these vaccines to DOH regional and provincial offices; and



- The Diarrheal Disease Control Program by producing part of the Oral Rehydration Solution (ORESOL) requirements of the program.

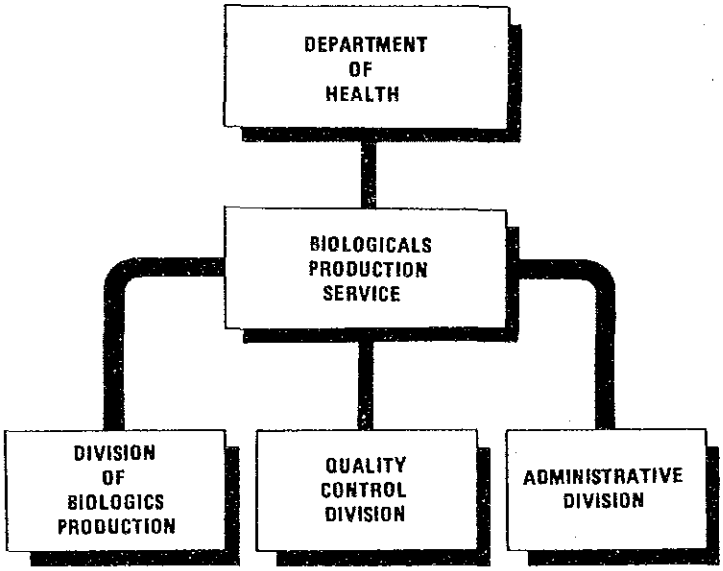
Additionally, the DOH Herbal Pharmaceutical Program with manufacturing facilities in four regions, namely: Region II-Tuguegarao City, Region VIII-Tacloban City, Region XI-Davao City, and Region XII-Cotabato City, has been placed under the control and supervision of the Assistant Secretary for Standards and Regulations with the assistance of the Chief of BPS.

The BPS is also mandated to provide support to other DOH agencies in the delivery of health services through the conduct of quality control test on all imported biological products before distribution to the public; and the production of antigen and antisera for diagnostic use of DOH or government laboratories.

ORGANIZATIONAL STRUCTURE

The reorganization of the Department of Health resulted in the separation of Alabang Serum & Vaccine Laboratory (ASVL) from the Bureau of Research and Laboratories making it an independent Service under the BPS. The ASVL is made up of three divisions:

Division of Biologics Production
Biologic Products Quality Control Division
Administrative Division

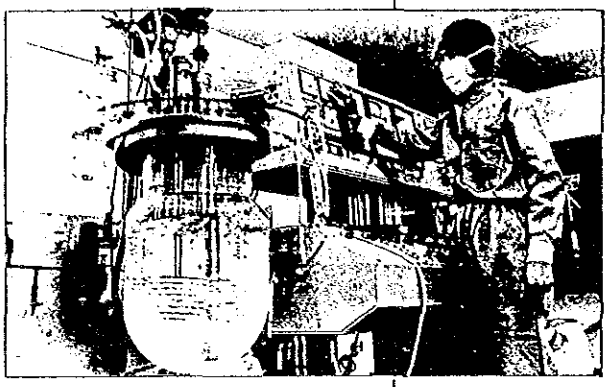


THE DIVISION OF BIOLOGICS PRODUCTION is concerned with the provision of quality vaccines for the Expanded Program of Immunization (EPI) of the DOH as well as vaccines and antisera for diseases. For this reason, the Division is composed of several laboratories specifically meant to answer the needs in BCG, tetanus, rabies, pertussis, diphtheria, cholera-media, and antigen.

THE QUALITY CONTROL DIVISION, which consists of the Quality Control Section and the Laboratory Animals Section, conducts quality control tests for all vaccines, both local and imported, before its release to the public. The Division is also concerned with the monitoring of activities of the production laboratories to determine conformity with the standards and requirements set by the World Health Organization and the Bureau of Food and Drugs (BFAD).

THE ADMINISTRATIVE DIVISION provides the BPS with efficient and effective services relating to finance, management, and maintenance. The Accounting, Budget, Cashiering, Personnel and Records, and the Supply and Property Sections, along with the General Maintenance Unit, make up this Division.

In September of 1988, Secretary Alfredo R. Bengzon issued Administrative Order No. 46 which states, among other things, that the BPS shall be under the direct administrative and technical supervision of the Assistant Secretary for Standards and Regulations.



BUDGET & EXPENDITURE

During its first year of operation, the BPS received a total allotment of P26,877,761.00 or more than a 100 percent budget increase over that of the previous year. Breakdown of allotment received is as follows:

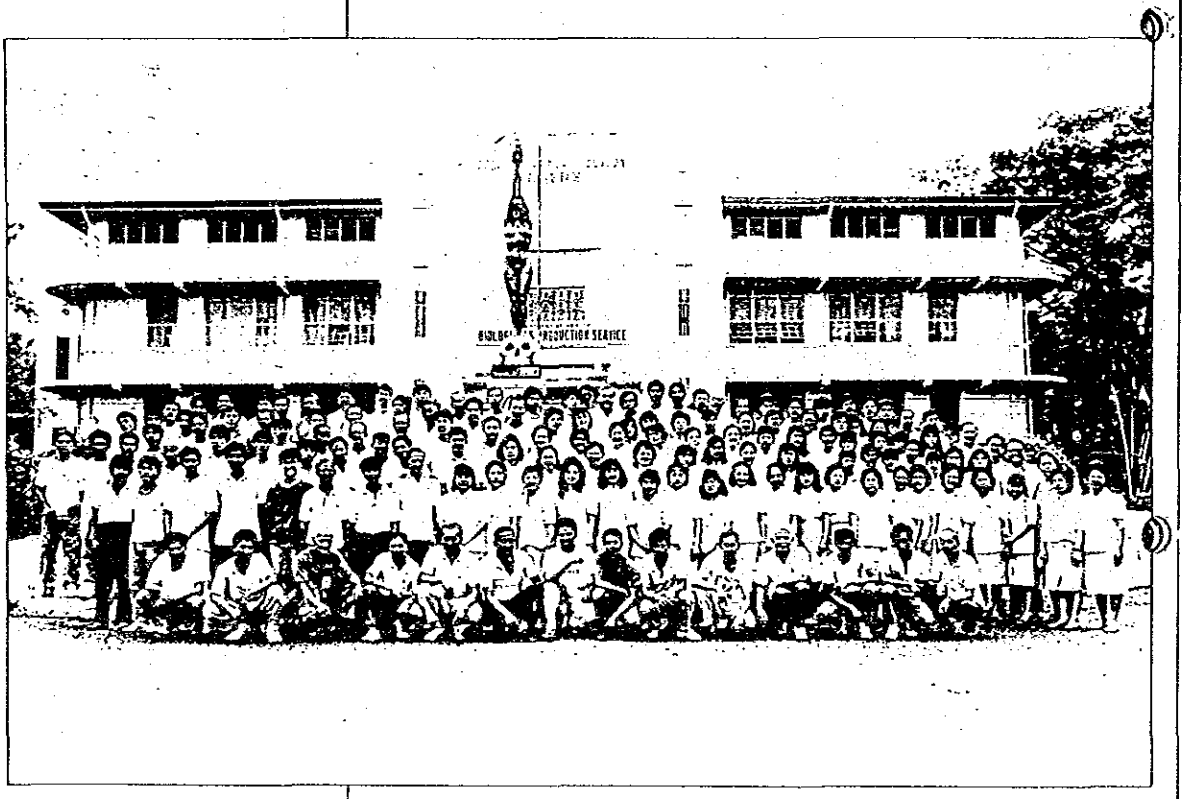
Personal Services	P 4,450,161.00
MOOE	18,880,000.00
Capital Outlay – Equipment	1,037,600.00
Capital Outlay – Infrastructure	2,510,000.00
	P 26,877,761.00

However, total expenditure during the period amounted to only 94 percent of the total allotment or P25,358,772.68. Distribution of expenses is shown below:

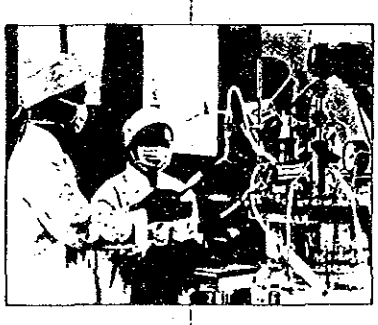
	PERSONAL SERVICES	M O O E	CAPITAL OUTLAY
Administrative Div.	897,247.78	5,042,489.49	1,973,581.05
		Total	7,913,318.32
Division of Quality Control	705,278.80	1,680,829.84	66,003.53
		Total	4,317,552.27
Division of Biological Production	2,570,718.90	11,952,567.69	470,055.60
		Total	13,127,902.09
TOTAL	4,173,245.48	18,675,887.02	2,509,640.18
		Total	25,358,772.68

PERSONNEL

The BPS has a total of 210 approved plantilla positions. Of this total: 185 are filled-up; 39 percent are professionals or college graduates, while the remaining 61 percent are either vocational, high school, or elementary graduates. Below is the list of professionals and educational attainment of BPS personnel:



A. Professionals	Number of Personnel
Doctor of Medicine	1
CPA	2
Pharmacist	10
Medical Technologist	16
Chemist	4
Engineer	1
	34
B. College Graduates	39
C. Vocational Graduates and those who had at least two years of college education	37
D. High School Graduates	51
E. Graduates and undergraduates of elementary course	24
TOTAL	185

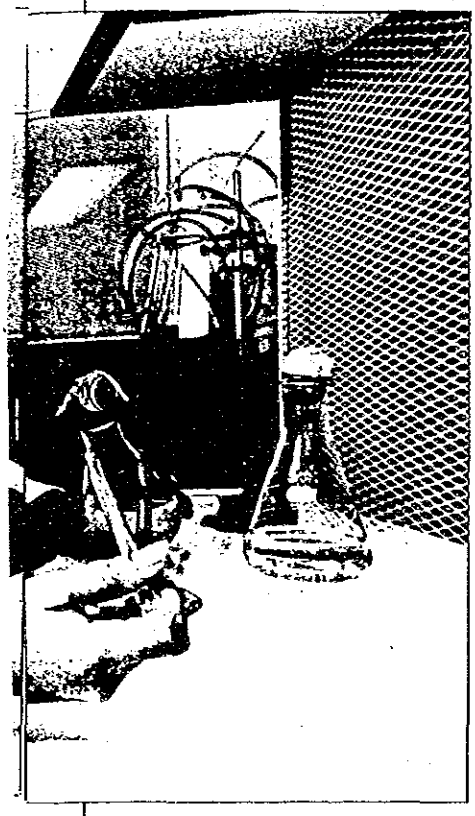


PERFORMANCE

Biologics Production Division

The production of the biological products is one of the primary functions of the Biologicals Production Service. The Division of Biologics Production is tasked with the provision of quality vaccines for EPI as well as vaccines and antisera for prevention of diseases such as tuberculosis, tetanus, typhoid, rabies, and the effect of cobra bites, as well as provision of antigen and typing sera for diagnostic services.

The Division also provides rabies vaccines for dogs as a support to the national program in the eradication of rabies in dogs being implemented by the Bureau of Animal Industry.



A. Stock Position of Vaccines, Sera, and Typing Sera:
As of 31 December 1988, the Division has released a total of 10,795,360 doses of vaccines and sera; 5,214 vials of antigen and antisera; 265,600 packets of ORESOL; and performed five trial combinations of DPT in small scale.

STOCK POSITION OF VACCINES, SERA, AND TYPING SERA
(As of 31 December 1987 and 31 December 1988)

Product	Stock on Hand Dec. 31, 87	Produced	Released	Stock on Hand Dec. 31, 88
	Vials / Doses	Vials / Doses	Vials / Doses	Vials / Doses
1. Vaccines & Sera				
a) BCG Vaccine	65,831	201,840	254,913	12,758
(20 dose amp.)	1,316,620	4,036,800	5,098,260	255,160
b) Tuberculin, 2TU	179	2,790	2,294	675
(75 dose vial)	13,425	209,250	172,050	50,625
c) Tetanus Toxoid	103,753	193,600	202,646	94,707
(20 dose vial)	2,075,060	3,872,000	4,052,920	1,894,140
d) Cobra Antivenin	439	750	861	328
(1 dose ampule)	439	750	861	328
e) Cholera Typhoid	5,923	16,766	20,115	2,574
(50 dose vial)	296,150	838,300	1,005,750	128,700
f) El Tor Vaccine	1,923	2,910	3,650[1]	1,183
(50 dose vial)	96,150	145,500	182,500	59,150
g) Typhoid Vaccines	360	285	399[2]	246
(50 dose vial)	18,000	14,250	19,950	12,300
h) 5% Rabies Vaccine	3,175	11,631	14,806	0
(14 dose vial)	44,450	162,834	207,284	
i) 5% Rabies Vaccine	3,175	11,631	14,806	0
(2 dose vial)	6,350	23,262	29,612	
j) 5% Rabies Vaccine	0	3,158	1,198	1,960
(16 dose vial)		50,528	19,168	31,360
k) Lep Rabies Vaccine	2,387	3,209	4,335	1,261
(2 dose vial)	4,714	6,418	8,670	2,522
TOTAL	3,946,817	9,359,892	10,795,360	2,435,950

Notes:
[1] *includes 100 vials expired.*
[2] *includes 95 vials expired.*

2. Antigen & Antisera				
a) Diagnostic Antigen				
Widal (50 ml/vial)	100	5,250	4,750	600
Weil Felix (50 ml/vial)	250	750	100	900
b) Diagnostic Typing Sera				
Salmonella (2ml/vial)	632	451	244	839
Shigella (2ml/vial)	46	317	50	313
Cholera (2ml/vial)	196	180	70	306
TOTAL	1,224	6,948	5,214	2,958
3. ORESOL		1,980,510	1,264,381	716,129
DPT				
a) Diphtheria				
Performed five trial combinations of DPT in small scale undergoing quality control test.				
b) Pertussis			Pooled Sample	
Pertussis Harvest	0	8,695ml	6,735ml	1,960 ml
Experimental Strain #134		(200 o.u./ml) or 99,365doses	(250 o.u./ml) or 76,965 doses	(200 o.u./ml) 22,400 doses
		(32 o.u./ml)	(32 o.u./ml)	(32 o.u./ml)
Pertussis Pool	0	12,705 ml	1,280 ml	11,425 ml
Experimental		(250 o.u./ml) or 145,250 doses (32 o.u./ml)	o.u./ml or 14,060 doses (32 o.u./ml)	(200 o.u./ml or 130,000 (32 o.u./ml)

B. Stock Position of Imported Vaccines

The EPI Unit handled the shipment and issuance of EPI vaccines consisting of the following: a total of 6,772,760 doses of DPT; 7,091,900 doses of polio; 2,247,710 doses of measles; 413,520 doses of BCG Japan; 5,059,820 doses of BCG local; and 4,018,160 doses of tetanus toxoid.

The Unit also took charge of the packing and shipment of rabies vaccine allocated to the different regions.

STOCK POSITION OF IMPORTED VACCINES

(As of December 1987 and December 1988)

Vaccines	Stock on Hand Dec. 1987	Deliveries Accepted EPI	Issued	Others	Stock on Hand Dec. 1988
	Vials / Doses	Vials / Doses	Vials / Doses	Vials / Doses	Vials / Doses
1. DPT Adsorbed	147,005	510,420	338,638	1,837	316,950
(20 dose vial)	2,940,100	10,208,400	5,772,760	36,740	6,339,000
2. Polio Vaccine	23,385	330,310	352,095	1,551	49
(20 dose vial)	467,700	6,606,200	7,041,900	31,020	980
3. Measles Vaccine	133,746	241,525	224,771	1,215	149,285
(10 dose vial)	1,337,460	2,415,250	2,247,710	12,150	1,492,850
4. BCG Japan	21,148		20,676	472	0
(20 dose vial)	422,960		413,520	9,440	0

C. Targeted and Actual Accomplishments, 1988

In 1988, the Division targeted a total dosage of 13,372,500 of vaccines and sera but produced only 9,359,892 doses; targeted 8,800 ml. of antigen and antisera as against the production total of 6,948 ml.

TARGETED AND ACTUAL ACCOMPLISHMENTS
1988

Activities	Target	Accomplishment in Doses	Accomplishment (in percent)	Loss
BIOLOGICAL PRODUCTS				
1. Vaccines & Sera[1]				
a) BCG Freeze Dried[2] (20 dose ampule)	6,000,000	4,036,800	67	0
b) Tuberculin (75 dose vial)	300,000	209,250	70	0
c) Cholera Typhoid[3] (50 dose vial)	1,500,000	838,300	56	0
d) El Tor Vaccine[4] (50 dose vial)	300,000	145,500	48	0
e) Typhoid Vaccine[4] (50 dose vial)	25,000	14,250	57	0
f) Tetanus Toxoid[5] (20 dose vial)	5,000,000	3,872,000	77	0
g) Cobra Antivenin[6] (1 dose ampule)	500	750	150	70
h) 5% Rabies Vaccine (16 dose vial)	240,000	236,624	98.59	(350 doses)
i) Rabies Vaccine LEP (2 dose vial)	7,000	6,418	91.68	0
TOTAL	13,372,500	9,359,892	69.99	70

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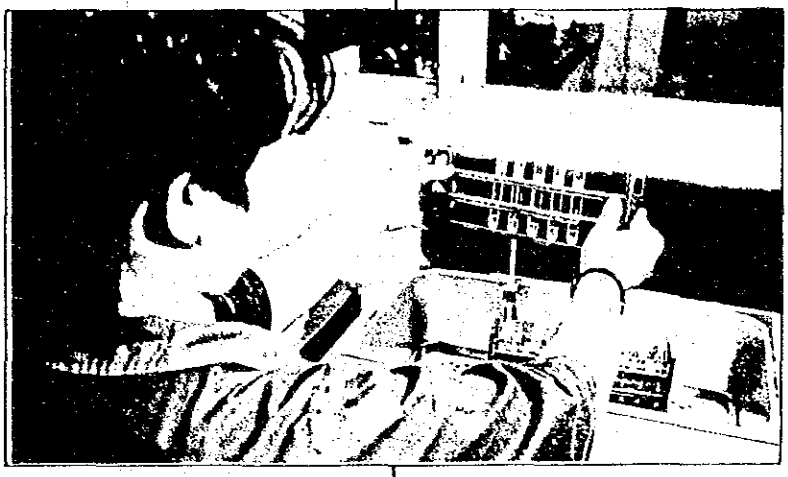
Activities	Target	Accomplishment in Doses	Accomplishment (in percent)	Loss
2. Antigen and Antisera				
a) Diagnostic Antigen				
Widal Antigen (50ml/vial)	5,500	5,250	95	0
Weil Felix Antigen (50 ml/vial)	1,000	750	75	0
b) Diagnostic Typing Sera				
Salmonella (2ml/vial)	1,500	451	30	0
Shigella (2ml/vial)	500	317	63	0
Cholera (2ml/vial)	300	180	60	0
TOTAL	8,800	6,948	78.9	0
3. Oresol Powder[7]	4,000,000	1,980,570	49.5	.0003
4. Pertussis in Bulk Products				
Pertussis Harvest Experimental Strain # 134 & 509	10,940 ml. (200 o.u./ml or 125 doses (32 o.u./ml)	15,290 ml. (200 o.u./ml or 174,720 doses (32 o.u./ml)	140	0
Pertussis Poll Experimental	10,940 ml (200 o.u./ml) or 125,000 doses (32 o.u. /ml)	12,705 ml (200 o.u. or 145,200 doses (32 o.u./ml)	116	



Activities	Target	Accomplishment in Doses	Accomlpshment (in percent)	Loss
5. Performance of Diphtheria Unit				
Adsorbed Tetanus Toxoid Final Bulk[8]	180 lots (5,760,000 doses)	126 lots (4,032,000 doses)	70	0.75
Aluminum Phosphate Suspension	180 lots	126 lots	70	0
Purified Diphtheria Toxoid[9]	10 lots	4 lots	40	20

Notes:

1 Produced vaccines still undergoing quality control tests:
BCG Vaccine Freeze-Dried (55,650 ampules = 1,113,000 doses)
CT Vaccine (3,000 vials = 150,000 doses)
Tetanus Toxoid (9,000 vials = 180,000 doses)

2 Production was way below target due to razing of BPS warehouse.

3 Production was temporarily suspended during 2nd quarter due to planned phaseout of CT Vaccine.

4 Sufficient stock of these two vaccines but less demand.

5 Dispensing was interrupted due to delayed results of Quality Control tests on final bulk.

6 350 doses failed in pyrogen test.

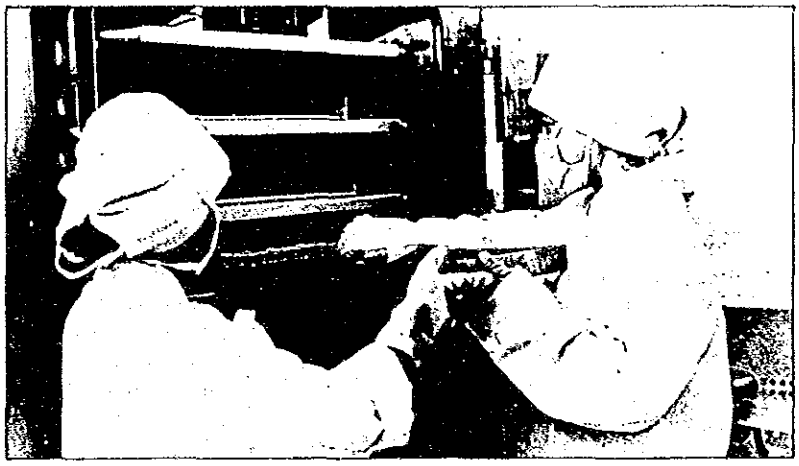
7 Production started in April and marred by frequent breakdown of equipment.

8 One lot failed in potency test.

9 One lot failed in purity test.

As of December 1988, the Division had:

- produced a total of 9,359,742 doses of biological products;
- released a total of 10,795,360 doses of vaccines and sera;
- produced a total of 6,730 ml. of diagnostic antigen and typing sera;
- performed a total of 277 different control tests in the Tetanus Laboratory;
- performed five trials of DPT combination;
- augmented a total of 4,450 liters of distilled water;
- washed and sterilized 102,973 pieces of 10 cc. vials;
- opened 506,000 packets of Oresol; and
- distributed a total of 20,676 vials of BCG Japan; 252,991 vials of BCG local; 1,200,908 vials of tetanus vaccines; 338,638 vials of DPT vaccines; 352,095 vials of polio vaccines; 224,771 vials of measles vaccines; and other kinds of vaccines outside the Expanded Program of Immunization (EPI) nationwide.



D. Impact/Effects of Accomplishments

Viewed on the totality, the Division has contributed its share in supporting the different programs of the BPS. It has produced a total of 3,872,000 doses of Adsorbed Tetanus Toxoid and 4,036,800 doses of BCG Freeze-dried vaccine allocated for EPI distribution.

Other vaccines released to support the program of control of specific diseases consisted of the following:

a) 20,115 vials of Cholera Typhoid vaccine capable of immunizing 1,005,750 people;
b) 3,650 vials of El Tor vaccine capable of immunizing 182,500 people;
c) 399 vials of Typhoid vaccine capable of immunizing 19,950 people;
d) 861 ampules of Cobra Antivenin equivalent to 861 doses capable of counteracting an equal number of people affected with cobra bites;
e) 16,004 vials equivalent to 256,064 doses of Rabies vaccine (16 dose vial) for human use; and
f) 4,812 vials of Rabies vaccine Lep equivalent to 9,624 doses capable of immunizing dogs against rabies.

E. Problems Encountered/Solution Undertaken

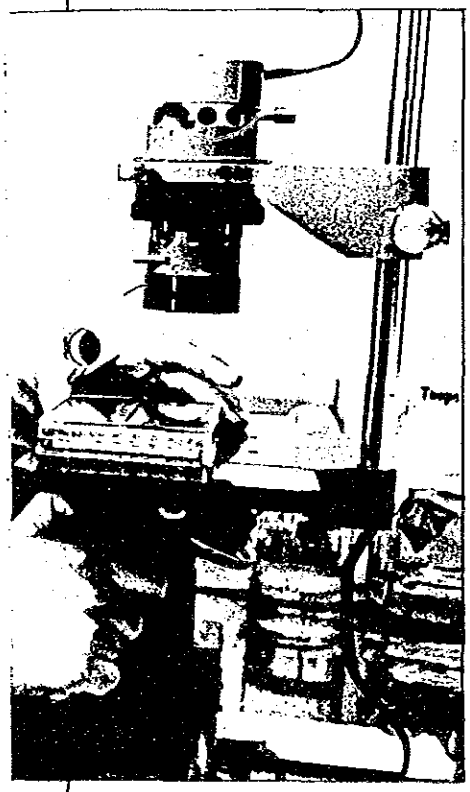
BCG Unit
- Diluent for freeze-dried BCG vaccine is still being done manually as the automatic filling and sealing machine has not been replaced

Tetanus Unit
- no steam supply during the months of January & February
- three lots of Cobra Antivenin Final Bulk failed in pyrogen test

Quality Control Division

The Biologic Products Quality Control Division performs quality control tests of biologicals produced or manufactured by the different production units of the Division of Biologicals. Its activities are independent of, but parallel with, the work programs submitted by the different production units. Samples representing each batch of vaccines and sera are tested for safety and efficacy in accordance with the Minimum Standard Requirements for Biologic Products by WHO Oresol Powder and

samples referred by the BFAD and EPI are also quality-control-tested. A release certificate is issued on every lot of biological after passing all the required control tests. This certificate is then signed and approved by the Chief of BPS.



A. TARGETED AND ACTUAL ACCOMPLISHMENTS, 1988

1. Quality Control Tests

The Division targeted a total of 10,430 quality control tests for 1988 and performed a total of 10,371 or a performance rate of 99 percent. Of the total, quality control tests were done on 376 lots; 202 sublots of bulk/final bulk/solutions/suspensions; and on 621 final lots and 122 sublots of products submitted.

Targeted and Actual Accomplishments
1988

Activities	Target	Accomplishments	Accomplishments in percent
Biologicals	3,950	3,910	98.9
Chemical	4,250	4,235	99.6
Physical	2,230	2,226	99.8
TOTAL	10,430	10,371	

Sample products are submitted to three kinds of control tests: biological, which make up 37.7 percent of the total number of tests; chemical, which make up 40.8 percent; and physical, which make up 21.5 percent of the whole process.

These control tests were performed on the following samples received in 1988.

Biological Product	Number of Lot/ sublot			Number of Lot/ Sublot		Number of Doses	
	Lot Number	tested	under-tested	passed	failed	approved	dis approved
1. Finished Products							
a) BCG Freeze-Dried vaccine[1]	8801 to 8831	31/31	22/22	8/7	1/2 8807-F; F1 (88-24)	3,996,000	–
b) Adsorbed Tetanus Toxoid, F.B.[2]	87-81 to 88-98	138	132	6	1 (88-72)	3,870.00	–
c) Cholera Typhoid Vaccine	880101 to 881112	12/56	10/47	2/9	–	838,300	–
d) 5% Rabies Vaccine Sample	87012-1,2,3 to 88004-1,2,3	16/31	16/31	–	–	238,493	–
e) Tuberculin Dilution	88-201 to 88-205[	5	5	–	–	157,125	–

Biological Product	Number of Lot/ sublot			Number of Lot/ Sublot		Number of Doses	
	Lot Number	under-tested	tested	passed	failed	approved	disapproved
f) LEP Rabies Vaccine	870015 to 870017	3	3	–	–	6,418	–
g) El Tor Vaccine	8805-2	1/4	1/4	–	–	145,500	–
h) PCAV[3]	8801 to 8804	4	2	–	2 (88001) (88002)	435	435
i) Typhoid Vaccine	880501	1	1	–	–	14,250	–
j) Oresol Powder[4]	0370 to 0219	312	297	–	15	–	–
k) BFAD Referrals[5]	–	87	72	12	3	–	–
l) EPI Vaccines	–	11	–	–	–	–	–
(Returned vaccines from Cebu: BCG, Tetanus Toxoid, DPT, Polio, and incoming imported vaccines DPT, Polio and Measles)							
2. Final Bulk/Products Solutions/Suspension							
a) AIPO[4] Suspension	01-88 to 126-88	124	124	–	–	–	–
b) Cholera Typhoid Vaccine	880202 to 881112	11/56	9/47	2/9	–	–	–
c) *Adsorbed Tetanus* Toxoid[6]	87-110 to 88-121	*136*	*113*	23	–	–	–
d) NSS	880201 to 881114	12/92	12/92	–	–	–	–
e) BCG Liquid Vaccine	Batch 8801 to Batch 8820	20	20	–	–	–	–
f) 40% Rabies Vaccine Concentrate	87020-A,B,C to 87026-A, B,C	7/14	7/14	–	–	–	–
g) 5% Rabies Vaccine A.D.	87014-1, 2 to 88005-1,2,3	15/29	14/27	1/2	–	–	–

Biological Product	Number of Lot/ Sublot			Number of Lot/ Sublot		Number of Doses	
	Lot Number	tested	under-tested	passed	failed	approved	disapproved
h) PCAV[7]	88001 to 88005	5	4	—	1 (88005)	—	—
i) Pertussis Pool	88-1 & 2 Strain 134 88-1&2 Strain 509 1-88 to 10-88	14	14	—	—	—	—
j) Purified & Concentrated Tetanus Toxoid[8]	87019 87020 87002 88002 88001 to 88006 87014	10	9	—	1 (88004)	—	—
k) El Tor Vaccine	8802-1	1/4	1/4	—	—	—	—
l) Purified Diphtheria Toxoid[9]	88001 88002 80-006 80-009 81-001 81-003 81-004 85-001 88-003 88-005 88-006	12	8	—	4 (failed)	—	—
m) Adsorbed Diphtheria Toxoid	Trial I	1	1	—	—	—	—
n) Adsorbed Diphtheria *Tetanus Toxoid*	Trial I *Trial II* A,B Trial III A, B	3/2	3/2	—	—	—	—

Biological Product	Number of Lot/ Sublot			Number of Lot/ Sublot		Number of Doses	
	Lot Number	tested	under-tested	passed	failed	approved	disapproved
o) DPT Vaccine	Trial I	5/5	3/1	1/1	1/3	–	–
	A, B						
	Trial II						
	A, B						
	Trial III						
	A,B						
	Trial IV						
	A, B						
	Trial V						
	A, B						

Note: 1 one lot failed in viability test
2 one sublot failed in sterility test
3 one lot failed in potency test
4 two lots failed in pyrogen test
5 15 lots failed in chemical composition
6 three samples failed in pyrogen test
7 one lot failed in pyrogen test
8 one lot failed in purity test
9. four lots failed in purity test

As of December 1988, the Biologic Products Quality Control Division had:

- conducted a total of 10,430 quality control tests;
- issued release certificates to biological passing control tests which has aggregate total of 9,440,172 doses;
- received an increased number of samples submitted by different production units as compared to 1987;
- noted a big drop in physical testing due to the fact that tests on Oresol samples was concentrated on salt mixture only during the first half of 1988;
- observed that during the 3rd quarter, samples from BFAD decreased since BFAD decided to perform pyrogen testing in their Bureau;
- expanded the animal house to accommodate the growing number of test animals; and
- conducted tests for five trial lots of DPT for potency.

Others:

- filled the position of Chief Research Bacteriologist on the third quarter; and
- media preparation for vero-cells maintenance still being done at University of the Philippines, Institute of Public Health, Manila for Measles and Polio vaccines titration.

B. IMPACT/EFFECTS OF ACCOMPLISHMENTS

Although there was a noted increase in incoming samples within the organization and from outside, the Division gave appropriate support to the work program of the different production units so that biologicals released for public use were within WHO standards.

Administrative Division

A number of unforeseen events, both natural and man-made, challenged the effectiveness of the Administrative Division during the early part of 1988. Among the more serious ones were the typhoon damaged steam boiler, a vital component in the overall performance of the organization; the burning down of the PBS Warehouse resulting in property damage of P10 M; delay in the release of funds; and the slow mechanism in the implementation of the DOH reorganization.

Despite the seeming insurmountable problems, the Division was able to render satisfactory service in terms of a) overseeing the reappointment of 143 personnel, recruitment of 37 qualified new employees, and the promotion of 23 deserving ones; b) payment of salaries on time and other personnel benefits; c) judicious use of funds; d) procurement of supplies, equipment, and materials at the lowest possible price; e) efficient maintenance of equipment and vehicles although majority are old; and f) submission of budget reports and other financial statements on time

Operational Plans

The Biologicals Production Service has its sights set across the century as it pursues its Short-Term, MediumTerm, and Long-Term Development Plans. These are:

1992 BPS aims to upgrade its facilities to higher technology standards, develop its manpower through training here and abroad, and achieve full production capability of DPT using a fermentor system.

1996 BPS intends to start production of Oral Polio and Measles vaccines and Vero-cell Derived Inactivated Rabies vaccines. It also seeks to pilot production of Oral Attenuated Typhoid vaccines by this time.

2000 BPS aims to start production of Hepatitis B vaccines and Polysaccharide vaccines. It also plans to achieve diversification to the manufacture of biological by-products at the turn of the century.

PRODUCTS

CHOLERA-TYPHOID VACCINE

COMPOSITION

It is a suspension of Cholera Vibrios of the El Tor Inaba and El Tor Ogawa and Typhoid (Ty_2) suspended in isotonic sodium chloride solution and preserved with 0.5 percent phenol. It is a heat-killed vaccine containing 4 billion organisms of El Tor Inaba; 4 billion organisms of El Tor Ogawa and 1 billion organisms of Salmonella typhin per ml. of the vaccine.

FREEZE-DRIED BCG VACCINE

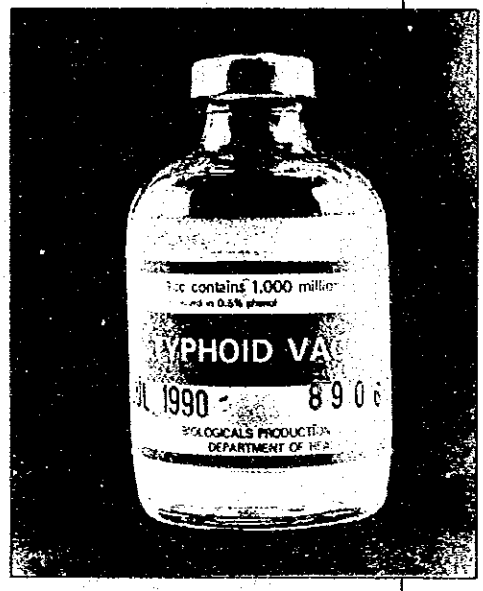
COMPOSITION

Freeze-dried BCG Vaccine is a dried preparation containing viable cultures of Bacillus Calmette Guerin stabilized in 1.5 percent sodium glutamate. It appears as dry light cream color powder. When reconstituted, it contains a minimum of 200,000 viable organism per 0.1 ml dose to induce tuberculin allergy in the vaccinated persons without undesirable reactions.

TYPHOID VACCINE

COMPOSITION

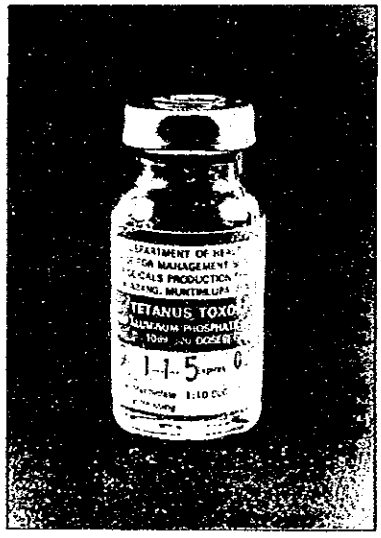
It is a sterile suspension of heat-killed salmonella typhosa organisms in isotonic sodium chloride solution with 0.5 percent phenol as preservative. Each ml contains 1 billion organisms.

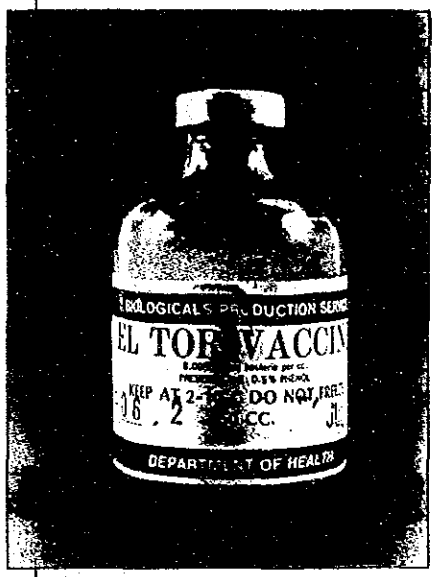


TETANUS TOXOID

COMPOSITION

Tetanus Toxoid is prepared from tetanus toxin detoxified with formalin, purified and concentrated, adsorbed with Aluminum Phosphate and preserved with 1:10,000 concentration of merthiolate.

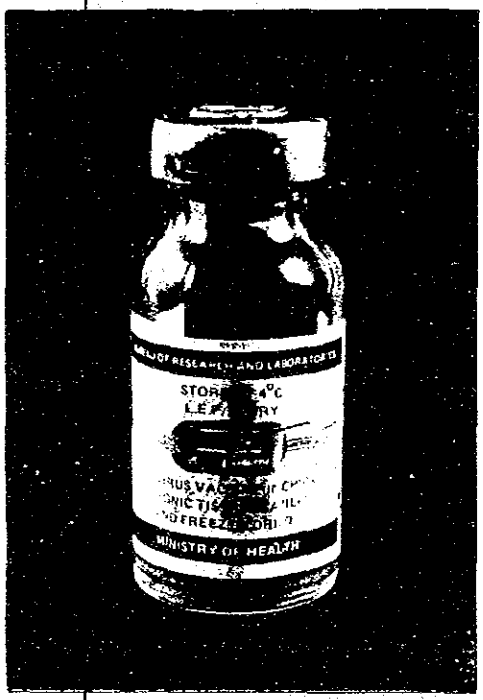




EL TOR VACCINE

COMPOSITION

It is a bacterial vaccine prepared from equal portions of suspension of cholera vibrious of the El Tor Ogawa and El Tor Inaba strains.
Each ml of the finished vaccine contains 8 billion organisms suspended in isotonic sodium chloride solution and preserved with 0.5 percent phenol.



LEP RABIES VACCINE

For dogs

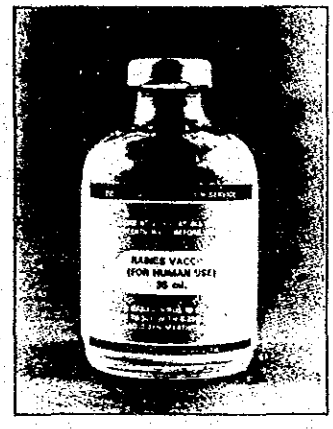
COMPOSITION

The vaccine contains an attenuated live LEP (low egg passage) Flury strain of rabies virus in 50 percent stabilized embryonic tissue suspension and freeze-dried.

RABIES VACCINE
For human use

COMPOSITION

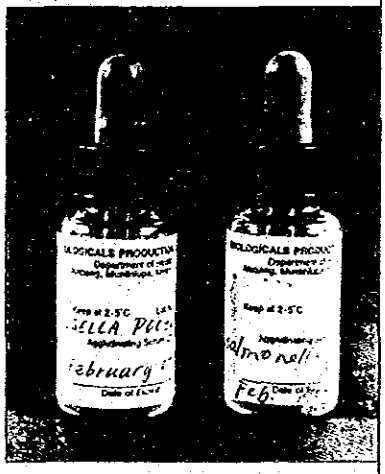
A single human dose of the vaccine contains not less than 2 ml of killed fixed rabies virus in 5 percent goat's brain tissue suspension in 0.25 percent phenolized sodium chloride solution preserved with 0.01 percent merthiolate.



AGGLUTINATING SERA

COMPOSITION

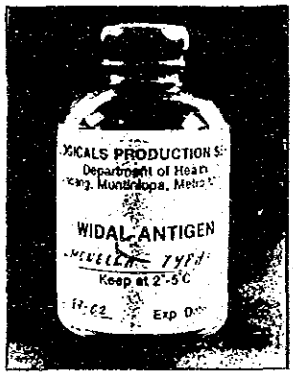
Salmonella, Shigella & Cholera Agglutinating Sera are prepared from rabbit's serum, made specific through absorption and preserved with merthiolate to a 1:10,000 concentration.



WIDAL AND
WEIL-FELIX ANTIGENS

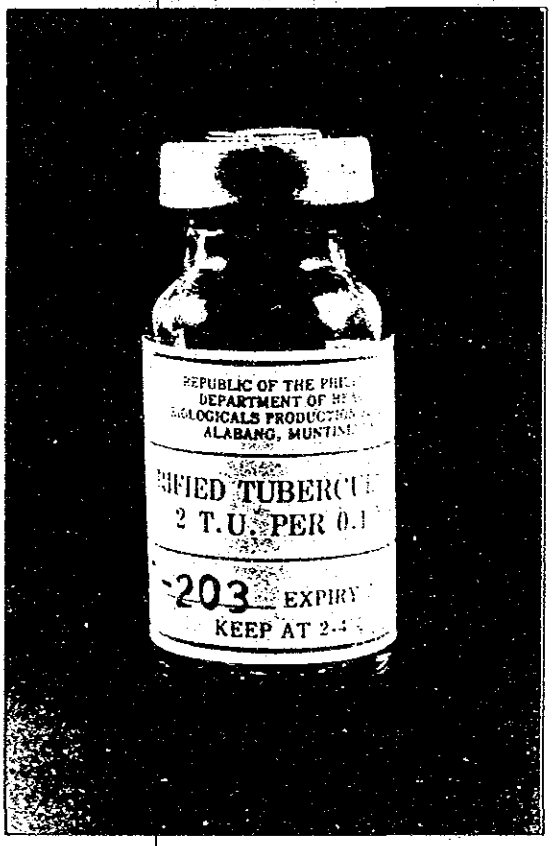
COMPOSITION

The product is more or less turbid, whitish liquid having a faint odor of phenol with a concentration of 400 x 10^6 org./ml. It is preserved with 0.5 percent phenol.



TUBERCULIN

Tuberculin is a preparation of Purified Protein Derivative (PPD) in form of stock solution containing 50,000 TU per ml of standard reactions obtained from Staten Serum Institute, Copenhagen.



Dilution of these tuberculin in phosphate buffer of the prescribed formulae -- 1 TU, and 5 TU with stabilizing diluent consisting of a 0.05 percent solution of Tween 80 in the diluent used hitherto, viz., phosphate buffered saline with 0.01 percent chinosol. The reason for introducing the Stabilizing diluent is that tuberculin prepared with ordinary diluent become adsorbed, to varying degrees, to the glasswares and containers in which the diluent is kept. This adsorption, which takes place rapidly plays a most important role in the attenuation of tuberculin dilutions. The adding of Tween 80 to the diluent prevents this adsorption and tuberculin dilutions prepared from RT 23 with Tween 80 diluent will cause stronger reactions than dilutions of the same unit-strenghts prepared with the ordinary diluent.

The use of Tween 80 provides three advantages:

a) much more stable and uniform dilution are obtained;
b) the specifically of the tuberculin dilution is increased, probably due to specific components of tuberculin being most liable to adsorption; and
c) the number of bullous reactions decrease (for reasons unknown).

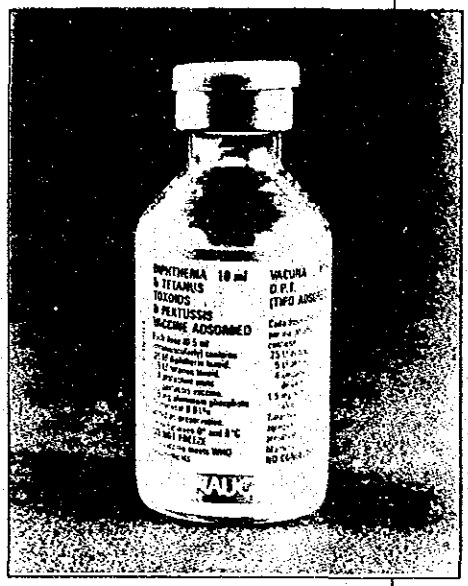
Tuberculin dilutions containing Tween 80 can be used for up to six months after preparation if kept cold.

Light and temperature has influence in the potency of the dilution. It is therefore desirable to prevent exposure of tuberculin to sunlight and heat. Dilutions are stored in bottles of brown glass and should always be refrigerated when not in used.

DPT ADSORBED

COMPOSITION

Diptheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (DPT Vaccine Adsorbed), is a sterile, cloudy, uniform suspension of Diptheria and tetanus toxoids and pertussis vaccine adsorbed on aluminum phosphate and suspended in isotonic sodium chloride solution. Each dose (0.5 ml) contains at least 30 IU (or 25 Lf) diptheria toxoid, at least 60 IU (mouse assay) (or 5 Lf) tetanus toxoids, at least 4 IU Pertussis Vaccine and aluminum phosphate (1.5 mg). Thimerosal 0.01% is added as a preservative. This vaccine fulfills the WHO requirements for Diptheria Toxoid, Tetanus Toxoid and Pertussis Vaccine.



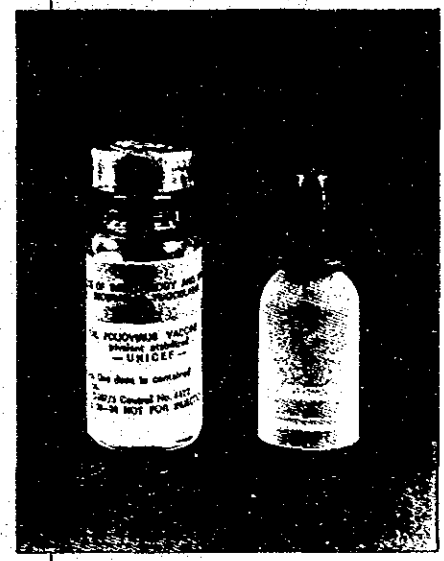
ANTIVENIN

Philippine Cobra Naja naja philippinensis, Anti-snake bite serum (equine origin)

COMPOSITION

This antivenin is the purified and concentrated serum of horses hyperimmunized with the venom of the Philippine Cobra (Naja-naja philippinensis) and preserved with 1:10,000 merthiolate.

It is generally issued in liquid form. When issued in freeze-dried form it is accompanied with a vial of diluency.



ORAL POLIO VACCINE

The Live Oral Vaccine (OPV) is a trivalent vaccine containing suspensions of types 1, 2 and 3 attenuated poliomyelitis viruses (Sabin strains). Each dose contains 1,000.000 TCID 50 of type 1, 1,00.000 TCID 50 of type 2 and 300.000 TCID 50 of type 3. The vaccine fulfills WHO requirements for Poliomyelitis Vaccine (Live) (WHO Technical Report Series No 329 1966 and Addendum 19[illegible] Annex 6, TRS No. 673, 1982).

Instant
ORESOL
(ORAL REHYDRATION POWDER)

FORMULA

Each packet contains:

Sodium Chloride	3.5 g
Trisodium Citrate dihydrate	2.9 g
Potassium Chloride	1.5 g
Sugar	40.0g

DIRECTIONS FOR MIXING

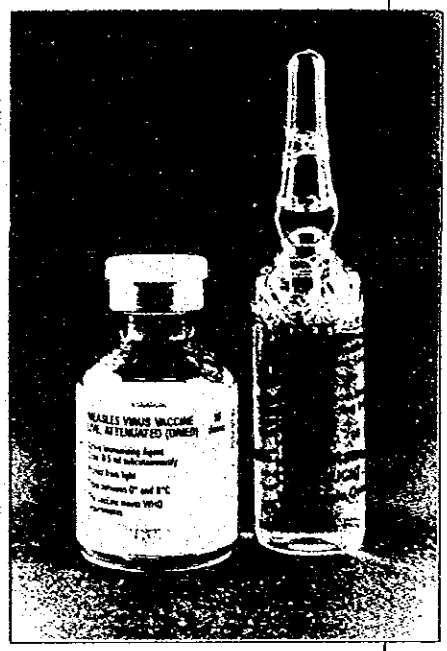
Measure 1 liter of drinking water in a pitcher, then dissolve the contents of the entire packet of oresol. AFTER EACH LOOSE STOOL, GIVE THE SOLUTION SLOWLY.

MEASLES VIRUS VACCINE, LIVE, ATTENUATED (DRIED)

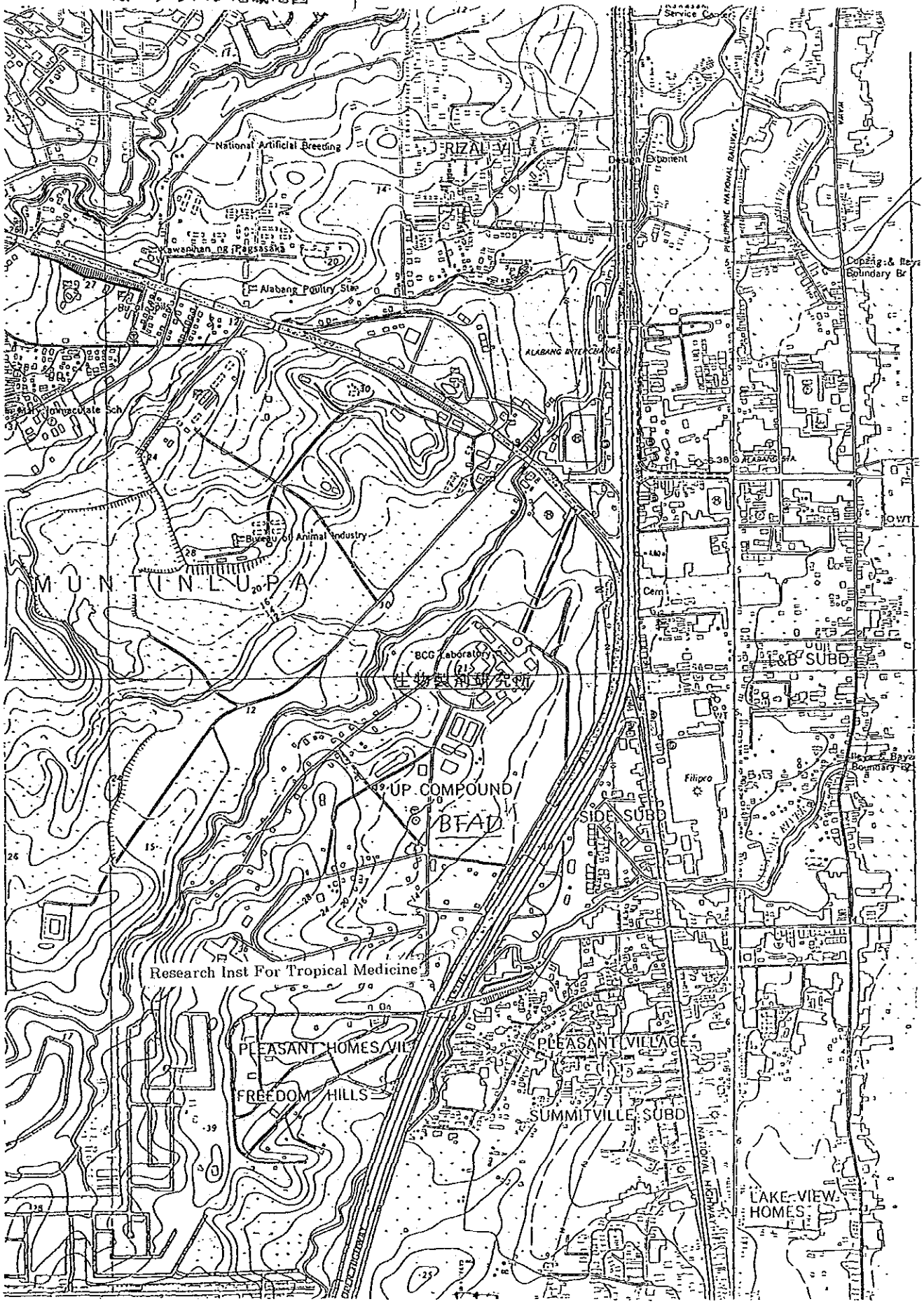
Active Immunizing Agent
For the Prevention of Measles (Rubeola)

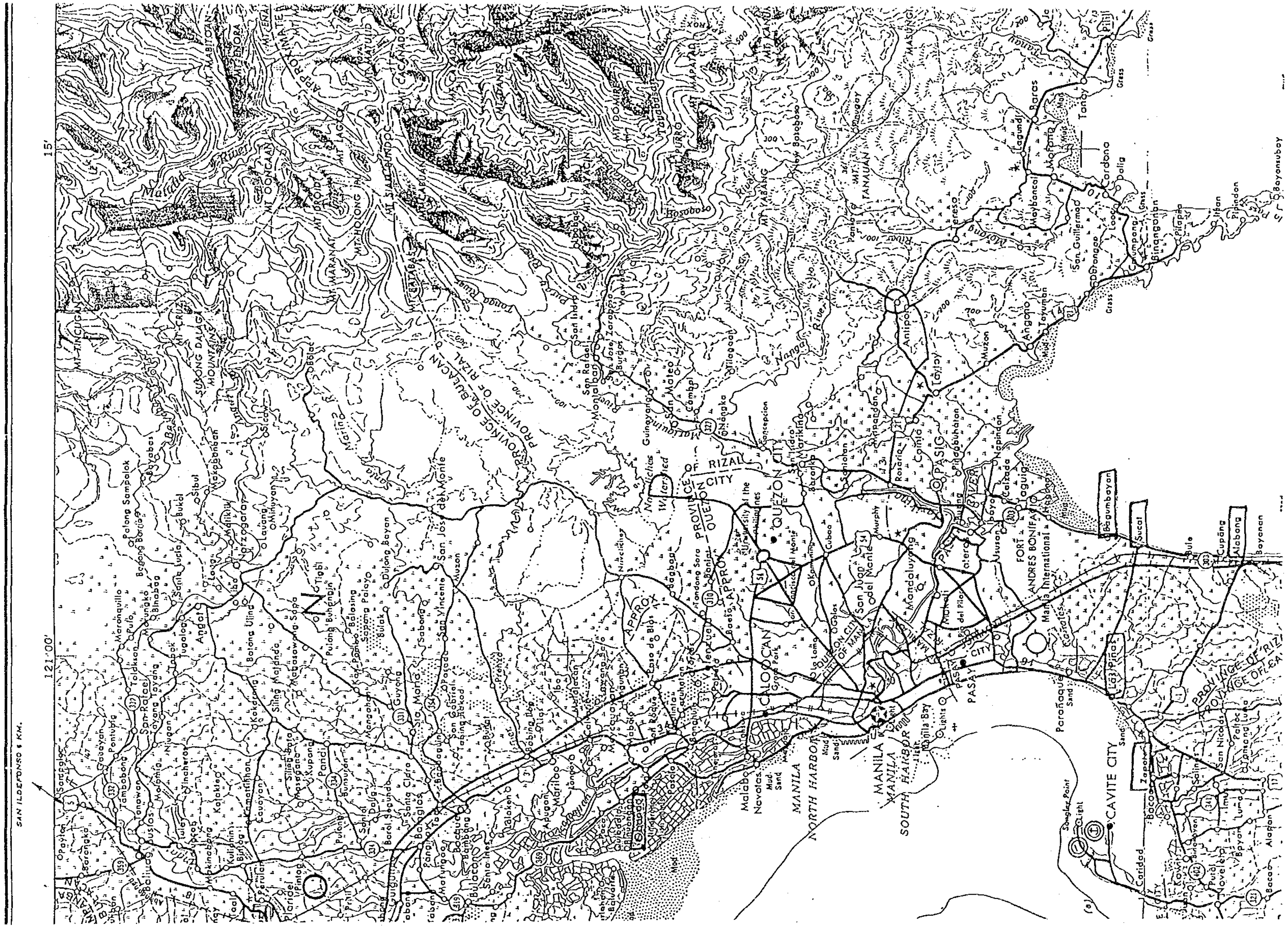
Measles Virus Vaccine, Live, Attenuated (Dried) is prepared in avian leucosis-free chick embryo fibroblast cultures from the Connaught strain, a strain of measles virus derived from the same original isolate as were other vaccine stains, such a [illegible]warz.[1,2] The Connaught strain was attenuated by sixty-nine passages in chick embryo fibroblast cultures.
The vaccine is freeze-dried in single-dose and multiple-dose vials. Each dose contains not less than TCID502 of measles virus and may also contain trace amounts of streptomycin, neomycin and polymixin B.

The vaccine fulfills the WHO Requirements for Measles Vaccine (LIVE)



13. アラバン地域地図


National Artificial Breeding
RIZAL VIL
Design Department
Service Co
Kawanihan ng Pagsasaka
Alabang Poultry Stn
ALABANG INTERCHANGE
Mary Immaculate Sch
Bureau of Animal Industry
MUNTINLUPA
BCG Laboratory
生物製剤研究所
UP COMPOUND
BFAD
SIDE SUBD
L&B SUBD
Filipro
Research Inst For Tropical Medicine
PLEASANT HOMES VIL
FREEDOM HILLS
PLEASANT VILLAGE
SUMMITVILLE SUBD
LAKE VIEW HOMES
ALABANG RFA
Cem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121°00'
15'
MANILA
NORTH HARBOR
SOUTH HARBOR
QUEZON CITY
CALOOCAN
PASAY CITY
PASIG
CAVITE CITY
FORT ANDRES BONIFACIO
PROVINCE OF RIZAL
PROVINCE OF BULACAN
Marikina
Mandaluyong
San Juan del Monte
Parañaque
Navotas
Malabon
Antipolo
Taytay
Angono
Binangonan

14. BPS予算

Republic of the Philippines
Department of Health
BIOLOGICALS PRODUCTION SERVICE
Alabang, Muntinlupa, Metro Mla.

C O M P A R A T I V E S T A T E M E N T O F A L L O T M E N T

Released

	1987	1988	1989
Salary	₱ 2,519,000.00	₱ 2,868,480.00	₱ 5,121,651.22
Cola & RATA	-	1,581,681.00	1,489,409.78
Maintenance & Other Operating Expenses:	8,623,000.00	18,620,000.00	20,663,000.00
Travelling	3,000.00	30,000.00	164,000.00
Communication	500.00	-	46,000.00
Freight	159,000.00	-	398,280.00
Other Services	688,000.00	984,651.00	1,139,718.00
Supplies & Materials	6,576,400.00	16,479,662.00	17,415,002.00
Power	1,100,000.00	968,363.00	1,000,000.00
Maintenance of Motor Vehicle	94,000	157,324.00	500,000.00
Representation	2,100.00	-	-
	₱ 11,142,000.00	₱ 23,070,161.00	₱ 27,274,061.00

CERTIFIED CORRECT:

ZENAIDA O. TAJARDON
Accountant III

Republic of the Philippines
Department of Health
Office of Management Services
BIOLOGICALS PRODUCTION SERVICE
Alabang, Muntinlupa

Comparison of Appropriation
for CY 1987 to 1990

	1987	1988	1989	1990
Personal Services	₱ 2,519,000	₱ 4,450,161	₱ 6,611,061	₱ 7,548,588
Maintenance and other Operating Expenses	8,623,000	18,880,000	20,663,000	22,694,000
Capital Outlay				
Equipment		1,037,600	2,423,650	815,000
Infrastructure		2,510,000	1,500.000	-
Total	₱ 11,142,000	₱26,877,761	₱ 31,197,711	₱ 31,057,588

15. ワクチン生産コスト試算

COST OF BCG VACCINE PER AMPOULE 20 doses

DIRECT MATERIALS			₱ 9.37
AMPOULES			
Amber	5.65		
White	3.50		9.15
LABELS			
Vaccine	.09		
Diluent	.072		.16
CHEMICALS/REAGENTS			.06
DIRECT LABOR			1.44
INDIRECT MATERIALS			5.52
INDIRECT LABOR			.65
OVERHEAD:			
Electricity		.37	
Quality Control			
Materials	.38		
Labor	.25	.63	
Fuel and Bil		.11	
Miscellaneous		.43	1.54
ESTIMATED COST PER AMPOULE			₱18.52

COST OF TETANUS TOXOID PER VIAL 20 doses

DIRECT MATERIALS	₱ 7.06
DIRECT LABOR	6.74
INDIRECT MATERIALS	2.49
INDIRECT LABOR	3.21
OVERHEAD:	
ELECTRICITY	1.84
QUALITY CONTROL	
MATERIALS	.60
LABOR	1.72
FUEL AND OIL	.55
MISCELLANEOUS	2.11
ESTIMATED COST	₱26. 32

COST OF RABIES VACCINE PER VIAL 16 doses

DIRECT MATERIALS	₱ 16.07
GOAT	
SODIUM CHLORIDE	
VIALS	
PHENOL CRYSTALS	
MERTHIOLATE	
DIRECT LABOR	25.57
INDIRECT MATERIALS	.38
INDIRECT LABOR	17.90
OVERHEAD:	
ELECTRICITY	10.23
QUALITY CONTROL	
MATERIALS	2.27
LABOR	6.44
FUEL AND OIL	3.08
MISCELLANEOUS	11.82
ESTIMATED COST PER VIAL	₱93.79

COST OF ANTIGEN PER VIAL 50 unit.

DIRECT MATERIALS		₱ 7.48
DIRECT LABOR		133.30
INDIRECT MATERIALS		.19
INDIRECT LABOR		83.64
OVERHEAD:		
Electricity	₱48.00	
Quality Control	-	
Fuel and Oil	-	
Miscellaneous	55.00	103.00
COST PER ~~VIAL~~ ڤيل		₱327.61

COST PER VIAL OF ANTISERA 50 units

DIRECT MATERIALS		₱ 6.86
DIRECT LABOR		192.55
INDIRECT MATERIALS		.19
INDIRECT LABOR		110.81
OVERHEAD:		
Electricity	₱69.00	
Quality Control	-	
Fuel and Oil	-	
Miscellaneous	79.00	148.00
COST PER ~~VIAL~~ sal		₱468.41

COST OF CHOLERA TYPHOID PER VIAL 50 units

DIRECT MATERIALS		¥ 7.13
DIRECT LABOR		18.48
INDIRECT MATERIALS		.61
INDIRECT LABOR		12.23
OVERHEAD:		
ELECTRICITY		7.03
QUALITY CONTROL:		
MATERIALS	1.82	
LABOR	6.57	8.39
FUEL AND OIL		2.10
MISCELLANEOUS		8.07
ESTIMATED COST PER VIAL		¥64.04

COST OF ANTIVENIN VACCINE PER AMPULE

1 doses

DIRECT MATERIALS		₱ 22.78
DIRECT LABOR		101.04
INDIRECT MATERIALS		48.00
INDIRECT LABOR		57.00
OVERHEAD:		
ELECTRICITY		33.00
QUALITY CONTROL		
MATERIALS	9.76	
LABOR	15.00	24.76
FUEL AND OIL		5.00
MISCELLANEOUS		19.00
ESTIMATED COST		₱ 310.58

16　ワクチン製造技術に関する調査結果

ワクチン製造技術担当　松　山　繁　夫

1．事前調査団の派遣（別途）

2．総　　括　　（別途）

3．要請の内容

3．1．ワクチン製造技術について

(1)　団長はプロジェクト技術協力（以下プロ技協）を前提とする調査団である事を繰り返し説明したが、ＢＰＳは、①バルク製剤を輸入し早期に純国産ワクチン生産の実績を作りたい。②ＢＣＧに例を挙げて事前のバルク生産拡大時の対応として、③輸入ワクチンより底コスト製品を獲得する手段として、などの理由で、製剤工程（Blending, Filling, Packaging,など）の無償資金供与（以下Ｇ／Ａと略）を諦め切れない様子であった。

(2)　Alabang地区にＧ／Ａで建設されたＲＩＴＭおよびＢＦＡＤとＢＰＳの現状との設備落差の大きさ、或はＵＳＡＩＤ報告書（Alabang Vaccine Complex : A Nedium Term Develoment Pian ; March, 1987.）、ＵＮＩＤＯ勧告（UNIDO Expert Panel : General Recommendation ; April, 1989.）などの諸提言を勘案すれば比側の要請も故なしとはしないが、①製剤工程はワクチン製造技術の中でもＧＭＰはより高度の技術のマネージメントを要する位置にあり、②さらに防腐剤（チメロサール、石炭酸、ホルマリンなど）を含まない生ワクチンの製剤工程は特に高度技術に属する、③まず細菌ワクチンの製剤経験を積み、当該工程の中央ユニット化と、そこに至る有機的マネージメント、内至システム化を会得すべきである旨述べた。

(3)　プロ技協の対象ワクチンとしてＢＰＳ側はＤＰＴとＢＣＧを採り上げたが、ＢＣＧについては品質管理（以下ＱＣ）は別として、①ＢＰＳで現に生産されている事、②本件製造技術は日本ビーシージーに属し、調査団の助言し得る範囲にないことを述べて、以後、ＤＰＴおよび破傷風トキソイド（以下Tn-T）に限定して協議する事で意見の一致をみた。

3．2．ワクチンの品質管理について　（別途）

3．3．ワクチンの検定について　（別途）

4．プロジェクト協力の基本計画　（別途）

5．プロジェクト協力の分野別基本計画

5．1．ワクチンの製造技術について

5．1．1．ジフテリアトキソイド（以下Di-T）

5．1．1．1．現状の把握

(1)　ファーメンター培養

深井報告（ＰＨＩＬ，ＲＰＴ，ＪＸＷ；June, 1989.）に述べられている通り、Di-Tファーメタンーは稼働していない。ファーメンター培養の製造フローチャートを求めたところ資料１のＷＨＯの「Example」が示された事から推しても、比国においても本機を使いこなすのは至難な事と見た。一般にファーメンター培養には、①問題を解決し、機械を使いこなすスキルが特に要求される。②条件吟味が多次元で難解である、③保守点検に要する部品（この場合輸入が主）を常備する、④電力、水、蒸留水などのサポートシステムを完備する、などの要求度が高いと言われ、比国の現状に沿わないように思われた。

無論、これ等の問題点を排除しファーメンターを稼働させる技術が国内、国外にあるかも知れない。その受け皿があるならばＢＰＳはその指導を受けるのがよい。

(2) 静置培養（ＢＰＳの現製造法）

製造フローチャートを資料２に示す。なお、ＢＰＳ試製ＤＰＴを日測で試験中である。日本での製造経験を比較して、①培地成分（特にFe）管理、②培養温度管理などの問題点が指摘され、基本的には、③工程管理手法としてLf単位測定を生産現場に持ち込み、④それにより問題解決のスキルを導入し、⑤培養工程、生成工程を組替えることでgrade-upは可能と思われる。

なお、現状は収率の概念を認識する迄には経験は至っていない。また建屋面積（資料３）に不足はないと思われる。

５．１．１．２．基本実施計画

５．１．１．２．１．基本的製造法の選択

(1) ファーメンター培養法

国内・国外にまだ隠れた技術があるかもしれないが、今次調査団としては、ＢＰＳでの早急なDi-Tファーメンターによるワクチン生産は困難と判断し、BPS側の静置培養方受け入れの可能性を打診した。

(2) 静置培養法

Di-T静置培養法は、①ＢＰＳはまがりなりにも本法を採用し（質的内容は別として）製造を試みている、②製造工程管理の指標となるLf単位に日比間の大きなバイアスはないようで（ＷＨＯ標準血清を直接使用し、ワーキング・スタンダードの持ちあわせがない）比側が日本の技術を認め易い、③ＢＰＳの現行製造法から見て、問題点が絞り易い、④必要器材（ガラスコルベン、など）が小さく、無菌性の維持、チェックなどの対応がとり易い、⑤日側の技術がＢＰＳで再現できるならば、世界的に十分通用する、あるいは水準以上の高品質品を提供出来る、⑥また、ＢＰＳの現状建屋面積で比側重要量を生産可能（算出根拠を資料４に示す）、などの理由から比側の早急なDi-T完成に対応するためには、静置培養法の改善がよりＢＰＳに適応し易いと判断した。

５．１．１．２．２．プロジェクト協力の可能性と方策

(1)　日本で経験した生産技術の忠実な再現を図る

試薬、製造装置類、ガラス器具に至るまで使用実績のある器材を可及的忠実にＢＰＳに持ち込む（何を搬送するかは未調査、少なくとも培養１バッチ相当器材、資金的な検討は未調整）。

問題点は（滅菌機用）蒸気と蒸留水の量と質にかかってくると思われる。

(2)　人・物・金・機械（４Ｍ）のチェック

今回は結論を得るに至らなかったが、日本での経験に徴して、菌培養のための恒温室の手直し、（ユーティリティを除く）蒸気滅菌機１台新設、など若干の手当でDi-Tバルク製造までの作業は進められるであろう。

(3)　技術の改善

技術改善の基本は安全性（無毒試験など）、有効性（Lf測定、力価試験など）にかかわる試験技術の質的、量的確保にある。ＱＣ技術の定着をまって、より比側の国情にあった器材、装置への置換を図りながら、技術改善合理化、原価低減に努める事が望まれる。

5．1．2．百日せきワクチン（以下Pt-V）

5．1．2．1．現状の把握

(1)　ファーメンター培養

深井報告（ＰＨＩＬ，ＲＰＴ，　ＪＸＷ：June，1989.）にある通り、今回調査団の訪問時にも運転中であった。しかし、製品完成までには至っていないと聞いたが、既にインドネシア国 Biofarmaの支援を受け（ＷＨＯ Consultant Report：（ＷＰ）ＬＡＢ，ＰＨＬ，ＤＳＥ，001-Ｅ；T. Usmadi，March，1989.）繰り返し試製が続けられている事を勘案すれば、国際的支援の立場からも、成ろうことならＢＰＳ製造法を完成すべく努めたい。

(2)　無細胞百日せきワクチン（以下A-Pt）

①副反応が強く、国際的にも使用者に不評な全菌Pt-Vを廃し、早急により優れたA-Ptを提供するのは道義的な立場からも望まれるところであり、さらには、②1981年以降、日本国内では全菌体Pt-Vの製造経験はない、③アルミ沈殿型DPTは国内で製造、品質管理の実績が全く無く、④（アルミ沈殿型ではない）全菌体DPT時代、Pt-Vの製造は安全性（モルモット安全試験など）と有効性（マウス力価試験）のぎりぎりの兼合いに技術者は異常な努力を強いられた苦しい経験がある、⑤またファーメンター培養法が比国での実現が難しくなった時の対応策とする、などの理由で本件プロ技協ではA-Ptの技術移転についても検討すべきと考える。

5．1．2．2．基本実施計画

5．1．2．2．1．基本的製造の選択

前項5．1．2．1．(1)の状態に鑑み、ファーメンター培養法を志向し、国内の支援機関を探索する。

一方、平行してA-PtのQC技術の移転を開始する。

5．1．2．2．2．プロジェクト協力の可能性と方策

(1) ファーメンター培養技術

ＢＰＳの現状の設備、技術を活かし、今一歩の改善を図るため、日側にある技術を結集して支援する。実現の可能性については今回の調査では結論を得るに至らなかった。

(2) A-Pt生産技術の移転

A-Ptの技術移転は当該ＱＣ技術の移転から開始すべきである。試製が続けられるであろうファーメンター培養技術の支援にも資するであろうし、A-Pt生産技術移転の前提として必須と考えるからである。ＱＣ技術の移転が確認されたところで、次期課題として生産技術の移転を検討する。ＤＰＴ完成のために跛行が生じた場合は、Pt-VまたはA-Ptの生産達成までの間、バルク輸入で対応する。

5．1．3．破傷風トキソイド（以下Tn-T）

5．1．3．1．現状の把握

(1) ファーメンター培養

ＢＰＳで意図している製造フローチャートを資料5に示す。訪問時には培養機は稼働していなかった。

問題点はDi-Tの事例と同じで、加えて精製用濾過器に見るように、基本生産設計が、大量培養、機械化優先、その結果低収率に落ちていると見られ、事態改善の困難さに拍車をかけている。Di-T同様、条件が揃えば十分に機能を発揮することが実証されている装置であるから、国内、国外に比側の現状を理解の上で、稼働させ得る受け皿があるならば好都合である事は論ずるまでもない。

(2) 静置培養法

ＢＰＳは現在静置培養法で作業を進めている。製造フローチャートを資料6に示す。なお、ＢＰＳ製品を日側で試験中である。

問題点は、①Lf測定用標準血清（自家製ワーキングスタンダード）の劣化又は疑反応によると思われるLf単位の過大評価の疑いがある、②Lf単位測定が工程管理に活かされてない、③日側で採用されている一般的静置培養法と比べて培養法、精製法、ともに可成りの相違が認められるなどの点にあり、改善の可能性が示唆された。

5．1．3．2．基本実施計画

5．1．3．2．1．基本的製造法の選択

(1) ファーメンター培養法

国内・国外にまだ隠れた技術があるかも知れないが、今次調査団としてはTn-TファーメンターをＢＰＳで早期に稼働させるには可成りの困難が伴うと判断し、ＢＰＳ側が日本で経験のある静置培養技術受け入れの可否について打診した。

(2) 静置培養法

ＢＰＳで現在進行中の静置培養法と日側で経験のある一般的製造法を比較すると、可成りの相違点が指摘される。①一般的にDi-Tに比較し、Tn-Tの静置培養法は仕掛けが一まわりが大きく、②作業条件の設定も道具建ての依存度が高く、また加えて、③ＢＰＳのLf単位は1/3～1/4の大巾なデノミネイションの必要性が予測される事から、ＢＰＳ技術の再建は必ずしもDi-T程容易ではないが、ファーメンター培養の複雑な条件設定よりはるかにＢＰＳの目標達成には近距離にあると判断された。また、日側の静置培養法の技術的経験がＢＰＳで再現出来るならば、④品質的に十分国際水準以上のTn-Tが提供されるであろうし、⑤量的試算値でも比国のＤＰＴおよびTn-Tの需要を十分生産可能と思われる（試算根拠を資料４に示す）ことから、静置培養法で質・量ともに比国の要請に答えられると思われる。

５．１．３．２．２．プロジェク協力の可能性と方策

(1)　日本で経験した生産技術の忠実な再現を図ること。

日側で使用経験のある試薬、培地原料、器材装置類など可能な限り比国に搬入して、ＢＰＳに日本の工程を再現する（何を搬送すべきか、また資金額についても未調査）

(2)　人・物・金・機械（４Ｍ）のチェック

今回は結論を得るに至らなかったが、作業場（資料３）の面積的には十分と思われ、①毒素とトキソイドをハードウェアの面で確保出来るようレイアウトを変える、②静置培養用にレイアウトを工夫する、③大型蒸気滅菌の新設（？）など若干の手当が必要となるであろう。

(3)　技術の改善

技術移転に不可欠なのは、ＱＣ技術、特にTn-TではLf測定技術の再研修と作業現場への（工程検査法としての）導入である。

①ＱＣ技術の確保をまって、②問題解決能力を附加し、③試薬、機材などの国産化、作業合理化、原価低減の諸改善を図るべきであろう。

５．１．４．製剤工程（ＤＰＴ、Tn-Tのアジュバント化以後包装までの工程）

５．１．４．１．現状の把握

ＤＰＴおよびTn-Tについて、アジュバント化以後の製造フローチャートを資料７に示す。

(1)　ＤＰＴ

試薬品の調製以外、実生産の経験がない。試製品についてＷＨＯでの検査を実施したとされるが、５ロットの中３ロットの不適理由を現場の担当者は知らないとの事であった。

(2)　Tn-T

16ℓ/ロットのアジュバント化済のバルクが冷蔵庫に保管されていた。

手作業で進め得るロットサイズは1,600本が限界なのであろう。ＢＰＳは品目毎に一貫作業としているので、Tn-Tの作業場が４つの建屋にまたがると担当者は嘆いていた。

5．1．4．2．基本実施計画

5．1．4．2．1．基本的製造法の選択

(1) 製剤工程担当部門の分離

上工程（培地調製・培養・精製・無毒化・濃厚原液までの工程）を一部門としてまとめ、下工程（アジュバント化・混合バルク・分注・包装）は分離独立するのが望ましい。①上工程と下工程では技術技能の質が異なる、②将来のＢＰＳの組織合理化（ＵＮＩＤＯ報告のユニット化）に備える、③役割分担の専門化により担当者の負担を軽減し、質的向上を図る、などの理由による。

(2) アジュバント化方法の選択

試験成績によれば、抗原のアルミゲル吸着率は　％であった。

アジュバント化法として吸着法（ＰＢＳ現行法）を採るか、沈降法をとるか、またゲルタイプをどのように設計するか、などは日側技術でも経験の分かれるところであり、支援担当技術者の経験に従うべきであろう。

5．1．4．2．2．プロジェクト協力の可能性と方策

(1) 現存の下工程機器（ミキシングタンク・分注機・まきしめ機・ラベル添付機など）の再評価

将来手狭になると思われるが、現存の機器レイアウトとしては作業面積は略々満たされている。問題は機械を使いこなす専門技術者、技能者の養成のないことであろう。一般に製剤工程機器はメインテナンス技術が不可欠で、その手当（問題解決能力）なしにはどんな高級な装置も動かすことは出来ない。ＢＰＳに現存する装置も日本の技術者ならば工夫改良して使いこなす一縷の望みはあるが、現在稼働していない具体的問題点が整理把握されておらず、稼働の可能性を判断するまでに至らなかった。

(2) 比国内医薬品メーカーの技術関係

ＢＰＳに現存する当該機器が稼働出来るか否か専門技術者の判断をまつ、もし不可となれば、比国内医薬品メーカーの既存設備を参考に設備設計を考えては如何と考える。

高級外国産機械よりも、比国内で実績のある機械の方が（それが仮に能力的に乏しくとも）製剤工程の早期機械化の早道であろうし、その経験を踏まえて問題解決能力向上を図るべきである。修理しようにも部品もない現状もこれによって解決するであろう。

もし、比国内に移転すべき機器、技術のない場合は希釈・分注・巻締め・包装の各工程を分割し、上流の工程から１工程から機械化を図り、下流の工程は機械化までの間手作業で継ぐ事となろう。

(3) 無償資金協力の必要性

ＤＰＴ、Tn-Tの量産が達成されると、年間分注本数は約70万本に達すると見られ、略々日本国内１社の製剤能力を具備する必要がある。加えて、将来麻しん、ポリオなどバルクを輸入し、製剤は国産化することを意図するならば、１ロット４万本の処理設備が

必要となり（Tn-TのＢＰＳ実績は1,600本／ロット）、本件プロジェクト技協と平行して、Ｇ／Ａの可能性検討も避けて通れないと考える。

(4) 人材養成

ＢＰＳには「製剤工程」の専門技術者、技能者はいないようである。

日側での長期研修により、①技術・技能の修得②問題解決能力の醸成③作業システムの把握④労務、原価など管理能力の賦与　などを修得した人材の養成が急がれる。

5．1．5．専門家派遣・研修員受け入れ・機材供与について

5．1．5．1．専門家派遣

(1) 日側の技術経験を比側が受け入れ、比国での技術再現を技術協力の具体的第１歩と位置づければ、専門家の派遣は重要な手段である。

特に、Di-T、Pt-V、Tn-Tのバルクの製造技術指導は専門家を派遣し、比国で実施するのがより効率的と思われる。

(2) 専門家派遣は長期であれ、短期であれ、多くの困難を併うであろう。ＢＰＬの固有事情を以下に例挙する。

① ＢＰＬは Metro Manila の１市である Makati 市の南約20km、South Super Highway の Alabang Interchange の近くに位置する（車で、朝15～30分、夕30～60分）。

② 良きにつけ悪きにつけ国際都市 Metro Manila の影響下にあり、派遣者の衣食住・交通・通信などの日常生活に不便はないと言う（日本との電話はダイヤル通信可、ファクシミリ可）。

③ 大使館、ＪＩＣＡ、ＷＨＯなどのオフィス所在地でもあり、派遣者の保健対策に不安はないと思われる。但し、国際都市の例に漏れず、あらゆる歓楽が手に入ると言われ、ＡＩＤＳ、肝炎の感染予防は特徴的課題と考える。ＢＰＳの唯一の喫煙場所はコブラ飼育室であった。

④ 治安は日本を除く諸外国並とも言われるが、住み易い環境とは見えなかった。

クーデターは比国民の安全枠とも言われ、日本のマスコミが取り扱う程比国民間では意義を感じていないようで、言うならば部族の争いと見るむきもある。これにより派遣者が身の危険に晒される事は考えられないと聴いた。

5．1．5．2．研修員受け入れ

(1) 本件プロジェクト技術協力の内容からして、①ＱＣ関連②製剤技術③マネージメント技術の技術・技能の移転は研修員受け入れがより効果的であろう。

(2) 一方、長年にわたる日比の技術協力、特に各種機関への研修員の受け入れにも拘わらず、ＢＰＳに技術の定着を見なかった、との反省も聞かれるが、①日本で研修した技術が活かされるような仕事に就いていないのでないか、②日本ばかりでなく世界各国で研修を受け、研修のための研修のきらいがある、③加えて、熟年女性の長と若干の中間層から成る人事構成が背景にあり、問題解決能力に乏しい。④研修技術を再生産する国

民性がない、などの理由によると考えられる。

(3) 対策として、①従業員の研修履歴と現状を分析し、実情を把握する、②帰国したら必ず日側で研修した作業に就労し、問題解決能力向上は急には求めない、③製剤工程の研修員には、使命感があり、やる気のある新人を複数登用する、④問題解決能力の向上は別途の組織化（技術支援部門の新設）を検討する、⑤ワクチン学の比側指導者をＲＩＴＭまたはＢＦＡＤに求める、⑥研修技術者、技能者のＢＰ外への流出は比国側が責任を持って歯止めをかける、などの処置が考えられる。

5．1．5．3．機材供与

(1) 蒸気配管の改修

現状は（理解出来ない事ではあるが）地中を断熱カバーなしに、剥き出し配管になっていると聞いた。最小限（仮設設備であっても）蒸気滅菌機に至る配管の改修は不可欠であろう。

(2) 蒸留水装置の新設

アラバン地域の水質（井戸水）はCaとFeイオンの多い硬質と聞く。既存のＢＰＳの設備は勿論のこと、ＲＩＴＭ、ＢＦＡＤの新設備でも当該装置は極めて幼稚な設備で、ＢＦＡＤの検査に支障をきたしている（ＪＩＣＡ宮本所長談）のも当然と思われる（無機質、有機質で汚染した水、容器で化学分析、病原微生物の分離・培養は困難である）。加えて、ＢＰＳの蒸気原水は地下水が直接使用され、配管にカスケードが生じている事から見ても、蒸気そのものが汚染していると考えられ、製造管理上も問題である。最小限、Di-T、Tn-Tの菌体培養に用いる培地、および培養装置類の洗浄には良質の蒸留水を供給する必要がある。

(3) 蒸気滅菌機

器具、装置の滅菌、培地類の調製、など無菌作業を維持する基幹機器である。ＢＰＳの現状では、蒸気の汚染も加わり、技術移転の隘路となることが懸念される。

是非、寄りどころになる滅菌機が必要となるであろう。

(4) ラミナーフロー・クリーンベンチ

外国から供与されたクリーンベンチが小型ながら必要台数揃っていた。

但し、その機能を果たしているかどうかの証拠は確認出来なかった。とりあえずこれ等のベンチを整備して局所無菌化システムで対応する工夫が必要となろう。

(5) その他の試薬、装置類

本件プロジェクトを担当する機関の経験した試薬、装置類（いづれも使用経験のあるものが望ましい）一式を比国に移送し、可及的忠実な再現を図る。恒温室、低温室（２～８℃）の改造も含め、今回は詳細調査未達となった。

6．提　言　（別　途）

7．その他：プロジェクト技術協力のTotal Strategy

7．1．日比バックアップシステムの構築

日側の経験を基に、比国の最も受け入れ易いと思われる技術をＢＰＳに出向いて再現する事は不可能ではない。しかし、それで技術が移転したと見ると早計であろう。途上国一般の例にもれず、口当たりが良く、話しは理解するが、行動力、問題解決力、技術の再生産に乏しいとするのは比国にも当てはまるかも知れない（ＷＨＯ、ＷＰＲＯ、梅内博士談）。

一方、本件プロ技協が進むとして、中核となるのはワクチン経験しか持ち合せのない技術者で相手国の国民性の改善にまで対応を求めるのは酷であろう。とすれば、プロ技協を成功させるためには、国民性の障壁を乗り越え得る仕掛けが不可欠となるであろう。以下に提言を例挙する。

(1) 使命感を分かちあい、技術的相談にも応じて頂けるプロモーターを日側に設定願い、カウンターパートとして、比側に次官以上のクラスのKey personを指名して、基本問題の解決に当たる。

(2) 外務省（ＪＩＣＡ）、厚生省（ＪＩＣＷＥＬＳ）、細胞製剤協会（各メーカー）の全面協力が得られる態勢をつくる。

(3) 5年以上の長期計画で進める。

(4) 技協の進展にあわせて、無償資金協力の支えを進める。

(5) 変化に迅速に対応出来るよう、専門家派遣、機材供与、資金供与に自由度を加味する。

(6) トラブル発生時の専門家派遣、応援など緊急対策も計画に組み込む。

(7) 比側に製造管理マネージャー（日本の薬事法の製造管理者に相当）を設置し、法的責任を付与する。

7．2．比国生産ワクチンの製造原価

ＢＰＳ提供の製品原価構成を資料8に示す。

7．3．プロジェクト技協の位置付けと年次計画案

資料9に示す。

以　上

ワクチン製造技術担当
高　橋　　隆

Ⅰ．技協プロジェクトは、D．T．P．三種混合ワクチンに品目を絞るとすれば次の様なことが重要課題となる。

1．D．T．については、日本側各ワクチンメーカーで製造されており、D．T．P．ワクチン用のD．T．の製造が可能である。それ故技協のプロジェクトが成り立つならば、即フィリピン側に技術移行ができる。

2．Pについては全菌ワクチンであり、それもタンク培養での製造であるため、日本側各メーカーもワクチン製造について確信を持っていない。全菌ワクチンについての不活化減毒工程の基礎研究がなされておらず、特にアジュバント添加製品（D．T．P．）については、日本側で製造が行われていなかった。そのため、P全菌ワクチンについては技術移行は不可能である。

3．フィリピン側でも不活化減毒法については確信がなく、D．T．P．ワクチン製造で数回欧米のワクチンメーカーへの視察を行い製造条件等の情報をかなり収集したにも係わらず、D．T．P．ワクチンの製造については確信を持っていない。

4．インドネシアWHOコンサルタントの協力によるタンク培養のP菌ワクチンに採用されている不活化減毒工程は、加熱およびチメロサール処理のみで毒性は高いと考える。

5．P全菌ワクチンに絞って言えば培養と不活化減毒に重点を置き、それらの毒性とワクチン力価の関連性について製造研究所が必須である。このため、P全菌ワクチン完成迄には長期の実際的技術協力が必要と考える。

6．D．T．P．ワクチンについては、WHO基準の毒性に関する試験に合格できるかが一番の問題となる。ワクチンの毒性と力価のバランスの点で、一定の製造工程が確立出来なければ製造は不可能であり、フィリピン側と共同で製造研究を行い製造工程の確立が必要となる。

Ⅱ．HBワクチンについて

1．HBワクチン製造については、製造を優先しているD．T．P．ワクチンが完成した後に実施する意向である、今の所、計画はされているが何ら準備されていない。製造計画では、1995年にHBワクチンの製造を完成したい様である。最初は、プラズマ由来ワクチンで出発する模様であるが、製造するとなると新しい専門の建物が必要であり、作業員の専門的なトレーニングも必要となるためフィリピン側の予算が取れるかにかかっている。

製造の方法については、日本側からの技術移行で完成出来る。

Ⅲ．専門家派遣について

1．ワクチン製造では製造工程を変えることは相当に困難なことであり、技協の専門家は、ワクチン大量製造を経験し、製造工程のチェック、現場作業、製造工程の確立が出来る者でなくてはならない。日本側の各メーカーでもその様な専門家が少ないのでないかと思われる。フィリピン長期滞在でも困難が予想される。

Ⅳ．機材供与について

1．ワクチン生産に必要な構造単純な機材を最小限に供与することが望ましい。それらは全てペアで供与し、付属消耗品のスペアの管理が出来るようにする。外国製品の場合でも修理が容易に出来るような機械、または修理者がすぐ来てくれる様な機械の供与が望ましい。

何ら複雑な高度の機械を供与しても生産に結び付かない事が今迄の他機関からの供与で明らかである。機械が充分あっても何ら生産に結び付かないことが多く、最小限必要な機材を充分活用出来ることが重要である。

現場での作業を行って見ないと必要な機材が判定出来ないので、専門家と現地部門との検討により決めることが最良と考える。

まとめ

1）技術協力を行うならば、目的としたワクチン製品を完成することが必須である。

2）現況設備を最大限に活用してワクチンの最大生産量を見極める。

3）目的とするD．T．P．ワクチンの内、特にP全菌ワクチンはフィリピン側と共同で製造研究を行う必要がある。

4）D．T．P．ワクチン製造については、基礎的研究を含めて長期実際的協力であり、非常に困難が予想されるが、充分な成果が期待出来るものと考える。

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Biologicals Production Service （ＢＰＳ）に於けるワクチン製造について

1．現　状

Expanded Program Immunization （ＥＰＩ）として使用されているワクチンはＢＣＧ、破傷風トキソイド、ＤＰＴ、ポリオ、麻しんである。その内、ＢＣＧ、破傷風トキソイドは、

Biologicals Production Service （ＢＰＳ）で製造供給されているが、ＤＰＴ、ポリオ、麻しんワクチンはカナダ政府より（コンノート社製ワクチン）援助を受けてＢＰＳはＤＰＴワクチンの試験製造を行っているが、まだ成功していないようである。麻しん、ポリオワクチンに関しては全く手がつけられていない。

２．ＢＰＳの目標

（短期的）

１）ＤＰＴワクチンの製品化及び破傷風トキソイドの品質向上

２）ＢＣＧの製造能力の強化

（中期的）

１）中央洗浄菌部門の確立

２）最終製品分注、巻締工程の中央化

３．調査結果

１）ＤＰＴワクチン

ジフテリアトキソイド、百日せきワクチン、破傷風トキソイド、それぞれの製造場所を設け人も設置して、破傷風トキソイドは製造、ジフテリアトキソイド及び百日せきワクチンは試験製造のレベルと思われるが、一応動いていた。

製造施設は、面積は十分と考えられるが、各部屋の使用方法は検討し、部分的な手直しも必要と考えられる。

マンパワーは、各部門のトップレベルの人達は知識としては十分持っているようであるが、未だ成功していないところを見ると、各方面からの情報に惑わされ、各工程の積重ねによる検討（工程管理）が不足しているのではないかと感じた。

２）ＢＣＧ

製品としてすでに供給しているが、最終工程の分注・溶封（アンプル）機は故障とのことで手動で行っていた。機械が修理不可能ならば、新設が必要と思われる。

３）中央洗浄滅菌部門

将来この部門をどのような目的で使用して行くのか、明確な考え方がないように感じた。ＧＭＰ的な考え方をするなら、むしろ、各部門に洗浄、滅菌設備をコンパクトに設ける方が良いと思われる。

４）最終製品工程（分注から巻締）の中央化

現状から中央化するためには、多額の投資が必要であり、現在、米国より供与された分注、巻締機ラインが全く使用されないで置かれている現状からすると、現時点での中央化は無理だと思われる。機械の取扱い、整備のできる人を育てる必要がある。その間は、簡単な機械で対応した方が良いと感じた。

5）麻しんワクチン

全く白紙の状態で、基礎技術、設備を全てこれから行わなければならない。そのためには数十億円の投資をしなければならない。

4．まとめ

今回ＢＰＳの調査に参加し、ＢＰＳの意見・要望によると、現在の問題点は、マンパワー、設備が不十分であることが強く、特に設備の充実により、各種ワクチンの製造が可能になるとの考え方が強いように感じました。確かに建物及び設備は老朽化しています。しかし、私は、設備を充実することによって、問題は解決しないと思います。それは、すでにユニセフからかなりの機器の供与を受けているにもかかわらず、殆どが使いこなされていない現状からすると、ワクチン製造に関する基本的な考え方、技術が乏しいためと思われます。

マンパワーについては、現在中心となっている人達は殆ど50歳前後の女性（資料ＢＰＳ staff参照）で、知識は十分にあるように見受けられますが、その知識で実際の担当者を指導し、問題を見つけ出し解決することが不足していることを強く感じました。この原因になっているのは、予算がないことから製造工程の見直しのための試験がなされていないことにあると考えられます。

以上のことからＢＰＳの改革は出来るだけ現状設備を利用して、少量でも高品質の製品を作り、マンパワーに自信をつけることから始めるべきではないでしょうか。その後で初めて国のポリシーに従った新しい施設の計画、実行が可能になると思います。

尚、当観音寺研究所で引き受けましたＢＰＳからの研修員ＪＩＣＡ生物製剤技術コース、62年度研修員１名、63年度研修員１名、64年角研修員２名及び64年ＷＨＯフェロー研修員１名は全てＢＰＳに在籍作業に従事していました。

以　上

ＢＰＳ　ＳＴＡＦＦ

ＢＥＲＮＡＲＴＯ　Ｔ．ＭＯＲＡ，ＪＲ，ＭＤ，Ｃ．Ｐ．Ｈ，

Director Ⅲ

Biologicals Production Service

Mr. Rodolgo B. Villarico

Administration V

Ms. PETRA B. LOJO

Bacteriologist V

OIC Biologicals Production

Chief Tetanus & Cabra Antiven Prod.

Ms. MARIA V. REDIMANO

Bacteriologist V

OIC, Quality Control

Ms. DOLORES M. MERCADO

Bacteriologist III

Chief, Robies Vaccine Production

Ms. ILMINADA CRUZ

Bacteriologist III

Chief, Diphtheria Vaccine Production

Ms. AUPARO SOBREMONTE

Bacteriologist III

Chief, Pertner's Vaccine Production

Ms. LEONORA E CRUZ

Bacteriologist III

Chief, BCG Vaccine Production

Ms. LOLITA. V. UMALI

Bacteriologist III

Chief, Cholera Medical Unit

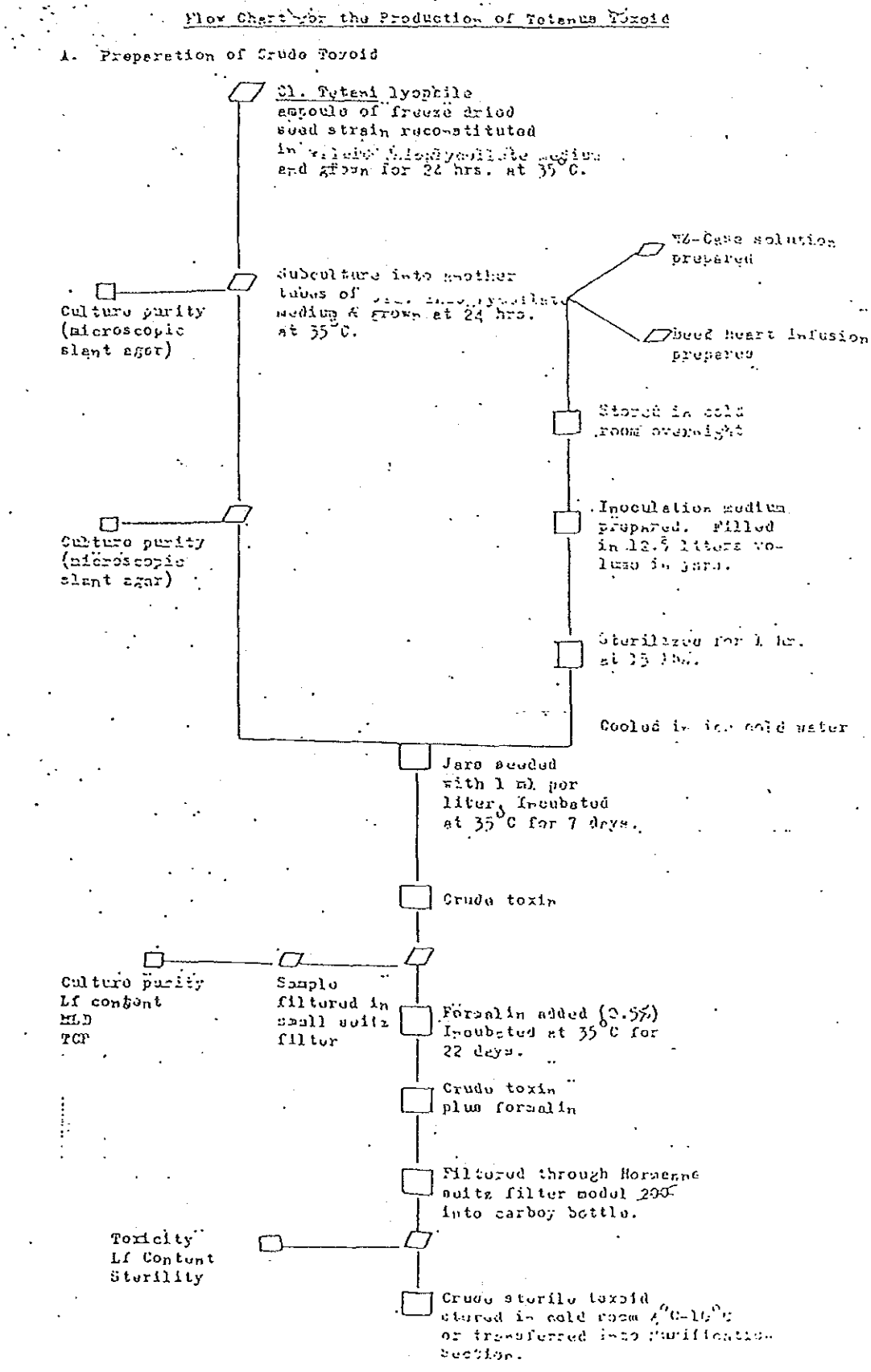
MR. MANUEL DANCEL

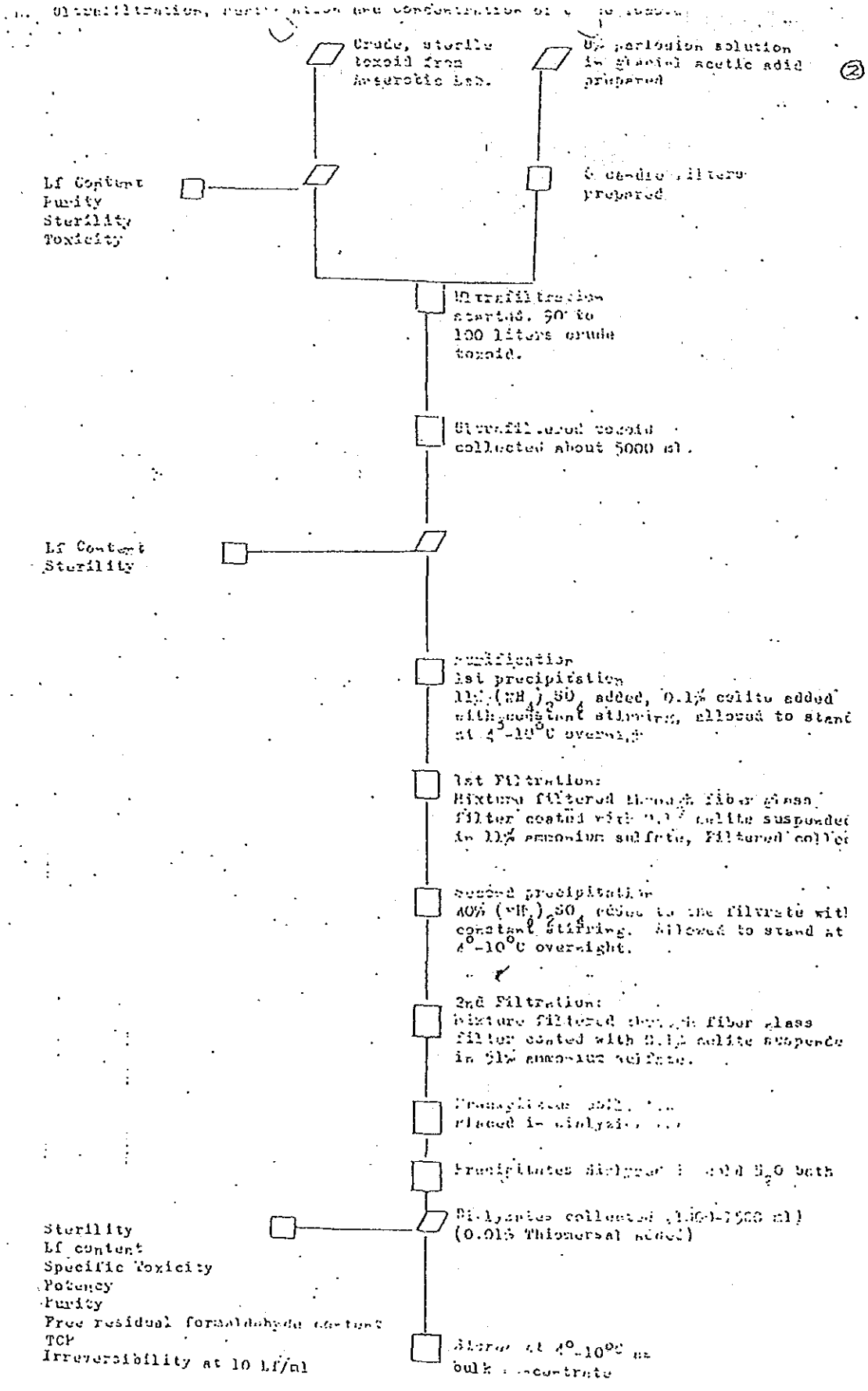
Production Bacteriologist

(Bacteriologist II)

Chief, Antiger. Anfisera Product

17. 破傷風トキソイド静置培養法




Ultrafiltration, purification and concentration of
Crude, sterile toxoid from Anaerobic Lab.
8% peptidion solution in glacial acetic acid prepared
2
Lf Content
Purity
Sterility
Toxicity
6 cardio filters prepared
Ultrafiltration started. 90 to 100 liters crude toxoid.
Ultrafiltered toxoid collected about 5000 ml.
Lf Content
Sterility
Purification
1st precipitation
11% $(NH_4)_2SO_4$ added, 0.1% celite added with constant stirring, allowed to stand at 4°-10°C overnight
1st Filtration:
Mixture filtered through fiber glass filter coated with 0.1% celite suspended in 11% ammonium sulfate. Filtered collected
Second precipitation
40% $(NH_4)_2SO_4$ added to the filtrate with constant stirring. Allowed to stand at 4°-10°C overnight.
2nd Filtration:
Mixture filtered through fiber glass filter coated with 0.1% celite suspended in 9% ammonium sulfate.
Precipitates placed in dialysis
Precipitates dialyzed against cold H_2O bath
Dialysates collected (1600-1700 ml) (0.01% Thimerosal added)
Sterility
Lf content
Specific Toxicity
Potency
Purity
Free residual formaldehyde content
TCP
Irreversibility at 10 Lf/ml
Store at 4°-10°C as bulk concentrate