CHAPTER 1. BACKGROUND OF THE PROJECT

(1) Background of the Request

In the "Strategy for Public Health Care and Protection in the Period 2001-2010", a review of the health care field during the past 10 years (1991 to 2000) was conducted. The Strategy stresses the importance of public health care policy and preventive medicine and sets the targets for public health care in 2010.

During the past 10 years from 1991 to 2000, there has been impressive progress in the public health care and medical field, despite Viet Nam undergoing a period of rebuilding the country. Especially in the field of preventive medicine, particularly suppression of infectious diseases through vaccine immunization, great success was achieved. This is largely attributable to the development of domestic production capabilities for all EPI vaccines (oral polio vaccine, diphtheria, pertussis, tetanus, tuberculosis, others) excluding measles. However, new problems such as increasing regional differences and appearance of gaps between social classes due to socio-economic development have developed.

Based on the above evaluation of the achievements of the past 10 years, the Strategy for Health Care and Protection 2001-2010 has set targets for 2010 as summarized below.

Table 1-1 Basic Targets in Strategy for Public Health Care and Protection

Target Items	Data for Year 2000	Target for Year 2010
Life Expectancy	67.8 years (based on 1999 statistics)	71years
Maternal mortality ratio of antenatal/ postnatal women	95 per 100,000 live births	70 per 100,000 live births
Infant mortality rate (under 1)	36.7 per 1,000live births (based on 1999 statistics)	25 per 1,000 live births
Under-5 mortality rate	42 per 1,000 live births	32 per 1,000 live births
% of infants with low birthweight (< 2,500g)	7.3%	Less than 6%
% of under-fives suffering from malnutrition	33%	20%
Increasing health workers	-	4.5 doctors and 1 university educated pharmacist per 10,000 population

(Source: Strategy for Public Health Care and Protection in the period 2001-2010)

In order to promote the smooth and early implementation of the Strategy for Public Health Care and Protection, a Decision by Prime Minister was promulgated on 19th March 2001. In the Decision, concrete directives were issued for establishing budgetary measures and organizations for policy implementation with the objective of providing primary health care equally to all citizens and to open the way for development of high quality health care services. Policies to improve the funding from various fiscal aid programs are to be

incorporated in the budgetary measures according to the Decision. During the period from 1996 to 1999, Viet Nam received fiscal aid amounting to approximately US$182,200,000. Of this amount, 38% was from international aid organizations, 50% bilateral aid and 12% from non-governmental organizations (NGO).

Under the National Objective Program for Control of Certain Social Maladies, Dangerous Epidemic Diseases and of HIV/AIDS in the period 2001-2005, 10 different programs were established to combat malaria, tuberculosis, dengue fever, AIDS, EPI target diseases and others. Each program was given specific target values to be attained in the program. The targets for EPI are listed below.

- morbidity of measles to be reduced to below 4 per 100,000
- immunization coverage of EPI target population to be maintained above 90%
- to maintain the achievement made in the eradication of poliomyelitis

A Decision by the Prime Minister dated December 13th 2001 has been issued to promote the smooth and early implementation of the National Objective Program.

The Government of Viet Nam has placed the reduction of the under-5 mortality rate and the suppression of outbreaks of infectious diseases as priority objectives under the Expanded Program on Immunization (EPI). The Government of Viet Nam intends to maintain the present high immunization coverage under EPI (DPT (Diphtheria, Pertussis, Tetanus) vaccine 96%, Measles vaccine 89%), while proceeding with the policy of developing sustainability in EPI vaccines (poliomyelitis, measles, diphtheria, pertussis, tetanus and tuberculosis). At present, all EPI vaccines except measles are produced domestically. Especially, poliomyelitis vaccine is being produced by Poliomyelitis Vaccine Research and Production Center (POLIOVAC). POLIOVAC is financially self-supporting and its production meets 100% of domestic demand.

Young children are particularly susceptible to measles and it also ranks as one of the leading causes of childhood mortality. Measles can trigger malnutrition and lowered resistance to infection for several months after infection. Immunization for measles is evaluated to be one of the most cost-effective health care interventions. The Regional Office for the Western Pacific of the World Health Organization (WHO/ WPRO), which is the regional office of WHO in charge of Viet Nam, is promoting the elimination of measles following the virtual eradication of poliomyelitis. Following this recommendation, the Government of Viet Nam has instituted a national program to control measles (Measles Control Program) that will conduct periodical mass immunization campaigns and an increase in the routine schedule to include a second dose of measles vaccination. This

will entail doubling of the required vaccine doses. However, manufacturers in developed countries are tending to move away from the production of low profit traditional EPI vaccines to higher value added vaccine production, causing rising concern in Viet Nam about supply stability in the future.

Following this development, Viet Nam has developed "The Project for Construction of Measles Vaccine Production Facilities" under WHO assistance and has requested the Government of Japan for Grant Aid cooperation for the construction of the production facilities with POLIOVAC as the base.

(2) Summary of the Request

The Summary of the request from the Government of Viet Nam during the Basic Design Study Stage is shown in the left-hand column of the Table 1-2 below. The items included in the Grant Aid Project after analysis are show in the right-hand column (underlines indicate changes from the original request).

Table 1-2 Summary of the Request

Facility Construction	Clean Rooms in Production Building (Bulk Production Section, Final Product Production Section) Air Conditioning Building Systems Plumbing Building Systems Electrical Building Systems
Equipment Procurement	Autoclaves (Bulk Production Section, Final Product Production Section), Hot oven, Freeze-drying machine, Vial washing machine, Dry-heat vial sterilizers, Vial filling machine, Aluminum capping machine, Labeling Machine, Cartoning machine, Line Synchronizing equipment

CHAPTER 2. CONTENTS OF THE PROJECT

2-1 Basic Concept of the Project

Measles is easily contracted by infants and is one of the leading causes of infant mortality. It triggers malnutrition and lowering of resistance to diseases for several months after infection and has a higher rate of morbidity even when compared to other vaccine preventable infant diseases. Viet Nam introduced a measles control program (Program for the Control of Measles) in 1981, which was subsequently expanded to cover the whole nation in 1985. Under this program, the reported cases of measles which was 82,000 in 1985 was reduced to approximately 6,000 cases 10 years later in 1995. However, there has been an increase in morbidity after 1997, with approximately 19,000 cases in 2000, even though the high coverage of immunization has been maintained. This is considered to be due to the fact that the measles elimination policy in Viet Nam has been conducted with one-dose routine schedule for infants.
Under these circumstances, the Government of Viet Nam has implemented mass measles immunization campaigns targeting all children and phased introduction of two-dose routine schedule for measles vaccination recommended by WHO/WPRO, with the intention to reduce the measles cases now showing a tendency to increase. This will entail doubling of the dosage requirements for measles vaccine. However, producers in the developed countries are moving away from relatively inexpensive EPI vaccines to higher value added vaccine production. This is raising concern about stability of supply in countries that are presently relying on imported vaccines, such as Viet Nam.
Furthermore, WHO/WPRO considers that Viet Nam has sufficient potential capability of producing international standard vaccines and bio-medical products and by establishing WHO compliant vaccine production control and quality standards, it will become possible for domestic production of measles vaccine.

The Project proposes to establish domestic production infrastructure of measles vaccine and provide a stable supply of measles vaccine, in order to elevate the self-sustainability of EPI program and the measles elimination program in Viet Nam.

In order to attain the above objective, the Project proposes to construct a measles vaccine production facility on a site in Than Tri District in Hanoi. The facilities are expected to strengthen the measles prevention measures of Viet Nam. Under the Project, the following facilities are to be constructed through Japanese-Vietnamese cooperation and to procure the necessary production equipment required for operation of the facility.

Table 2-1 Summary of the Cooperation Project

	Vaccine Production Building (3,116m^2)	Animal Laboratory (358 m^2)	Mechanical Building (484 m^2)	Ancillary Buildings
Japan	Bulk Production Zone Final Product Production Zone Quality Control Zone	Animal Test Zone	Procurement of Building Systems equipment and Installation	
Viet Nam			Architecture & Structure	Administration Building, Canteen, Guardhouse, Incinerator, Parking Garage, others

The portion to be implemented by Japanese side (the Cooperation Project) is composed of the following.

1. Vaccine Production Building
   - Bulk Production Zone: Reception of SPF Eggs· Incubation, Cell Culture, Virus Culture, Media Culture, Media Preparation
   - Quality Control Zone: Aseptic Testing, Cell Testing, Chemical testing
   - Final product: Production Zone: Final Bulk Formulation, Vial Filling·freeze-drying, Capping, Visual inspection, Labeling, Packaging, Delivering
2. Animal Laboratory: Animal Testing rooms
3. Mechanical Building: Building system equipment for Mechanical Room (boiler, refrigeration machines, pumps), Transformer Room, Generator Room

The architectural finishing and structure for the Mechanical Building is to be constructed under Vietnamese funding. Ancillary buildings, such as Administration Building, Canteen, Parking Garage, Guardhouse and landscaping as well as in-site road construction are also to be constructed by Vietnamese budget in concordance with the construction schedule for the Japanese portion.

2-2 Basic Design of the Requested Japanese Assistance

2-2-1 Design Policy

(1) Basic Policy

1) Basic Policy for Design of Facilities

i. To construct vaccine production facilities in compliance with WHO-GMP.

ii. To minimize the possibility for occurrence of human errors in the process of operation by securing isolation of quality control facilities and providing separate animal laboratory building.

iii. To prevent cross-contamination and loss of quality by designing clear and rational zoning and layout of functions and equipment.

iv. To develop an appropriate production environment and design a production system that will ensure high quality of products.

v. To provide rationally designed facilities that will not have excessive operational costs.

2) Basic Policy for Design of Building Systems

The premises for production of measles vaccine are appropriate cleanliness in production environment and stable supply of production water and electrical power. Therefore, careful consideration of the quality of city water and power supply will be taken in the design of the building systems for clean rooms required to comply with WHO-GMP standards. Furthermore, efforts will be made to incorporate energy conservation in the design.

3) Basic Policy for Equipment Procurement

Equipment procurement will be based on the basic policy to provide the minimum required equipment necessary for the production of 7.5 million doses of measles vaccine annually. Ordinary equipment items that that can be procured in Viet Nam (lockers, racks and consumables) shall be procured by the Vietnamese side

4) Basic Policy for Soft Component Planning

Validation and technical assistance for operation and maintenance of the facilities and equipment will be provided under the Soft Component Scheme as part of the Japanese Grant Aid cooperation, in order to ensure the proper operation and maintenance of the facilities and equipment in compliance with WHO-GMP standards.

5) The relation with Technical Assistance

The full production of measles vaccine will require the development of personnel capabilities of the staff who will be responsible for the operation of the measles vaccine production facilities and the transfer of production process and quality control technology.

Therefore, continuing efforts to implement the following necessary items will be made through discussions between concerned officials of Japan, Viet Nam and WHO.

i. Training and internship in production and quality control for POLIOVAC personnel by Kitasato Institute.

ii. Human resource development for production and quality control by experts from WHO designated training institutes.

iii. Assistance to develop the capabilities of the national regulatory agency (NRA).

(2) Natural Conditions and Building Design

1) Wind

The city of Hanoi belongs to the temperate monsoon zone and experiences easterly winds of around 3 m/s throughout the year. The layout of buildings on the project site is on the east/west axis in order to lead the wind into the site and provide adequate ventilation between the facilities. The placement of the Animal Laboratory will be carefully planned to minimize smell pollution of neighboring areas by animal odors.

2) Rainfall

Rainfall in the Hanoi area is concentrated in the rainy season, during which 90% of annual rainfall is observed. Maximum rainfall in Hanoi is high as 200 mm to 400 mm per day and 100 mm per hour. Therefore, due consideration must be taken in the design of the roof drainage and the determination of the capacity of the on-site drainage system.

3) Temperature and Humidity

Average temperature in summer, which is from June to September in Hanoi, ranges between 28 degrees to 30 degrees. Highest average monthly temperature in summer can be as high as 30 degrees centigrade. Relative humidity is over 70% throughout the year. Therefore, air-conditioning equipment will require large capacity. In order to reduce the heat load, the buildings will be designed with insulation layers.

4) Daylight and ultraviolet radiation

Hanoi is located at latitude 21 degrees north and receives high angle sunlight at noon. Therefore the roof construction should have good thermal insulation. The buildings are laid out so as to avoid larger perimeters facing west, where the incoming solar energy is maximum.

5) Earthquake

The Building Code of Vietnam requires incorporating the seismic force into the structural design. The structural design for the project is calculated with consideration of appropriate seismic loads to the buildings.

6) Soil Conditions

The Production Building is designed to be two stories high and has higher than usual ground pressure. As it is difficult to distribute the weight of heavy production equipment evenly throughout the building to achieve a balanced plan and the possibility of uneven settlement due to the relatvely low bearing force of the ground, bored pile foundations are designed for the structure of the Production building.

The underground water level has been recorded to be almost as high as the ground surface level, so all substructure such as underground pits will be carefully designed to prevent water intrusion.

(3) Policy Toward Socio-Economic Conditions

Vietnam has experienced a long period of warfare on their own land and many other historical difficulties, which have left the nation behind in economical development such as seen in other ASEAN nations. A reform and liberation policy called the “Doi Moi” policy was introduced in 1986 with the aim of initiating economic development by providing state owned enterprises with self initiative powers and encouraging foreign direct investment in the country. However, residual weakness in basic management resources, social infrastructure, et cetera still remain. On the other hand, there are many strengths of Vietnam worthy of respect, especially in the well-organized socialistic network and the diligence of its people.

Therefore, the basic policy in the implementation of the Project will be to provide appropriate advice to the Vietnamese side to establish a project implementation organization capable of timely decision-making and to achieve efficient operation of the Project, taking into consideration the above socio-economic conditions.

(4) Policy Toward Local Conditions for Construction/Procurement and Business Practice

Basic construction technology as well as construction tools and machinery have been accumulated in the past with the support from the Soviet Union. The capabilities of local contractors have improved considerably through increased number of joint projects with foreign companies following the economic liberation. Construction firms from Hong Kong, Singapore, Korea, Japan, Germany, et cetera, have formed joint ventures with local contractors mainly to carry out foreign investment projects. Through technology transfers and mechanization of construction in such projects, local construction firms have achieved considerable levels of capabilities and now cranes, lifts and ready-mixed concrete trucks are frequently found at large scale construction sites of 14 to 20 story buildings in Hanoi.

(5) Policy Concerning Utilization of Local Subcontractors

The capabilities of local subcontractors generally are at a considerably good level. However the adjustments and networking of various trades and works are not necessarily performed properly and efficiently and the systematic coordination of related works at the project site such as between architectural and mechanical components are not conducted consistently as a whole, leading to costly delays and errors in the construction. Strong leadership and good coordination will be required when local subcontractors and traders are utilized.

(6) Policy Concerning the Implementation Agency's Organizational Capabilities for Operation and Maintenance

The engineers and staff of POLIOVAC, the nominated implementation agency for the project, have the expertise for production of biological/pharmacological products , but they have no experience in the production of measles vaccine. Especially, technological assistance is necessary for implementation of the Project and detailed discussion between relevant parties should be commenced from the basic design stage.

(7) Production Capacity of the Proposed Facilities

Based on the assumption of implementation of the EPI target of two-dose routine schedule for measles vaccine, the target population for the initial dose is 2.4 million per year (including 1.8 million infants and 0.6 million children in high-risk areas such as mountainous districts) and 2.4 million (including 1.8 million 5 year olds and 0.6 million children in high-risk areas) for the second dose, for a total of 4.8 million (infants and children). To this figure, adjustments are made for loss due to underdeveloped cold chain

system and actual yield figures for NIHE (50%), resulting in 7.2 million doses per year as the required annual production dosages. Further adjustments for the mass measles eradication campaigns held every 3 to 4 years and the follow-up needs make the requirement 7.5 million doses per year.

Table 2-2 Annual Requirement of Measles Vaccine by Year

Year	First Immunization				Second Immunization				Total (doses)
	Newborns under 1	Infants 1 to 2 years (HRA)*	Loss factor (%)	Req. amount (doses)	Infants 5 years	Children 5 to 10 years (HRA)	Loss factor (%)	Req. amount (doses)	Total Req. amount (doses)
2005	1.8 million	0.6 million	50%	3.6 million	1.8 million	0.6 million	50%	3.6 million	7.2 million
2006	1.8 million	0.6 million	50%	3.6 million	1.8 million	0.6 million	50%	3.6 million	7.2 million
2007	1.8 million	0.6 million	50%	3.6 million	1.8 million	0.6 million	50%	3.6 million	7.2 million
2008	1.8 million	0.6 million	50%	3.6 million	1.8 million	0.6 million	50%	3.6 million	7.2 million
2009	1.8 million	0.6 million	50%	3.6 million	1.8 million	0.6 million	50%	3.6 million	7.2 million
2010	1.8 million	0.6 million	50%	3.6 million	1.8 million	0.6 million	50%	3.6 million	7.2 million
2011～2020 **	1.8 million	0.2 million	50%	3.0 million	1.8 million	0.2 million	50%	3.0 million	6.0 million

Note: HRA*: High Risk Area
** This number shows the annual target population and the annual requirement
(Data from National Institute of Hygiene and Epidemiology (NIHE), Ministry of Health)

(8) Policy Concerning the Selection of Production Equipment and facility dimensions

The minimum necessary equipment and facility dimensions for production lines having adequate capacity for the production of 7.5 million doses of measles vaccine annually will be selected and designed. The selection of equipment is based primarily on considerations for the specifications, prices and availability of post-installation services with further considerations for technical and economical self-sustainability and expandability. The individual equipment selection will take into consideration ease of handling, durability and ease of operation and maintenance. The analysis regarding local suppliers and agencies have found that locally available refrigerators for storing starting materials, reagents and final products are already widely used in Viet Nam. Furthermore, it was confirmed that the procurement and maintenance of consumables and QC equipment in Viet Nam would present no problems, although consumables required for the trial running of equipment will be provided by the Japanese side.

(9) Policy Concerning Construction/Procurement and Period of Construction

1) Construction Methods

The whole area around Hanoi is composed of thick layers of soft clays and silt 30 to 40 meters deep, generally requiring pile foundations. Most newly built large-scale developments and buildings with foreign investments have adopted pile foundations, but many local buildings of medium height or lower are built with direct foundations.

The superstructure commonly uses reinforced concrete frame structure with brick fill-in walls.

There are restrictions on traffic of construction vehicles and construction work time (nighttime and holidays) within the city area of Hanoi. However, the Project site is located outside the Hanoi city area and the above restrictions do not apply and the effects on the construction schedule for the Project are deemed to be negligible. At present the landfill and grading of the site have been completed as well as fencing works. However, the installation of utilities such as electricity and city water has not yet commenced. Confirmation with responsible public work corporations on the implementation schedule for the infrastructure is required for the utilities to be completed in coordination with the Project construction schedule under Vietnamese funding and that no delay effects the completion or operation of the Project facilities.

2) Basic Policy for Procurement of Materials and Equipment

The study of market conditions for main construction materials have found that except for a few items almost all materials and equipment can be procured locally. At present, materials and equipment of various quality and standards from Europe, Russia, China and other countries are available on the local market. Locally procured materials will be selected as often as it is possible to facilitate ease of repair, operation and maintenance after construction, but available quality and quantity will be confirmed to prevent adverse effects to the construction schedule.

(10) Measles Vaccine Production Planning

The measles vaccine production planning was studied from both the measles vaccine production process and the production environment requirements.

The measles vaccine production process is first designed by planning the composition of the production equipment based on the production process and next adding the planning for quality control functions.

The production environment plan consists of the planning of the building, air-conditioning system, and electric equipment systems. In planning production system utility service systems are also required for supporting the production facilities.

1) Production process

Measles vaccine production process is composed of bulk production process, final product production process, inspection and packing process and processing of production water. Each process is composed of sub-processes described below:

i. Bulk production process
   a) SPF eggs manufacturing
   b) SPF eggs incubation
   c) Cell culture
   d) Virus culture
   e) Final bulk composition (formulation equipment)

ii. Final product production process
   a) Vial and stopper washing and sterilization
   b) Vial filling
   c) Freeze drying
   d) Capping

iii. Inspection and packing
   a) Vial collecting and visual inspection
   b) Labeling
   c) Packing

iv. Production water processing system
   a) WFI production and supply system
   b) Pure steam production and supply system
   c) UFW production and supply system

The particular specification of each production equipment was decided based on the production process provided by production process licensor. For this purpose, production capacity, unit flow and process flow, main equipment composition and operation timetable was established under assistance of the process licensor or a

specialist engineering firm in the field of medical products. Based on this process information the specification of each piece of equipment including the composition, numbers, capacity, material and level of automation was determined. The resulting production equipment list in combination with the process plans and production environment specifications which were finalized at the same time, are the given conditions for planning the production environment.

In addition to the above process, quality control of intermediate products and final product are required. This process requires the provision of testing rooms and animal laboratories. The animal laboratory will require separate air conditioning system and effective insect and rodent control management in order to comply with WHO-GMP requirements.

2) Planning of production environment

The planning of production environment is divided into two categories as follows:

i. Building and site planning

Building and site planning provide enough space for the installation of all the production equipment and necessary space for their proper operation and control. In planning the buildings and the site, consideration for compliance with GMP requirements are incorporated to achieve prevention of cross-contamination and meeting the requirements for workability, cleanability, air-tightness, and chemical resistance. GMP requirements are specified for each production process.

ii. Air-conditioning system planning

Air-conditioning systems must provide the required contamination control in compliance with WHO-GMP and proper temperature and humidity required by operators and products. WHO-GMP standards stipulate the cleanliness of the production process and zoning of the facilities. Gowning rules in compliance with requirements of WHO-GMP are also planned. Air-conditioning system, zoning, type of filters, ventilation rate, temperature and humidity are specified as required by above plans.

3) Utility service systems

Utility service systems are of secondary priority under WHO-GMP. However, they are important systems supporting the production equipment. The project includes the following equipment:

- Water processing and supply system (including reception of city water to pretreatment and supply of processed water to production equipment)
- Chilled water supply equipment
- Boiler equipment
- Pressurized air generator
- Sewage treatment equipment
- Power receiving and transformer equipment

4) Supply of SPF eggs

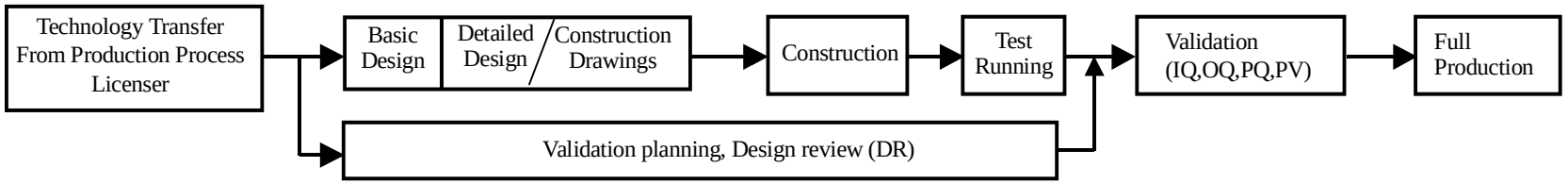
It is planned to import SPF eggs from SPAFAS of the United States of America. BIO-FARMA was also considered as a possible supplier, but it was planning to expand production for its own needs and notified the Study Team that it had no additional capacity to supply SPF eggs to other countries.

POLIOVAC is planning to produce SPF eggs by themselves in the future. Therefore, this project will reserve a certain open space in the site for the construction of the building and facilities to produce SPF eggs in the future.

5) Technology transfer

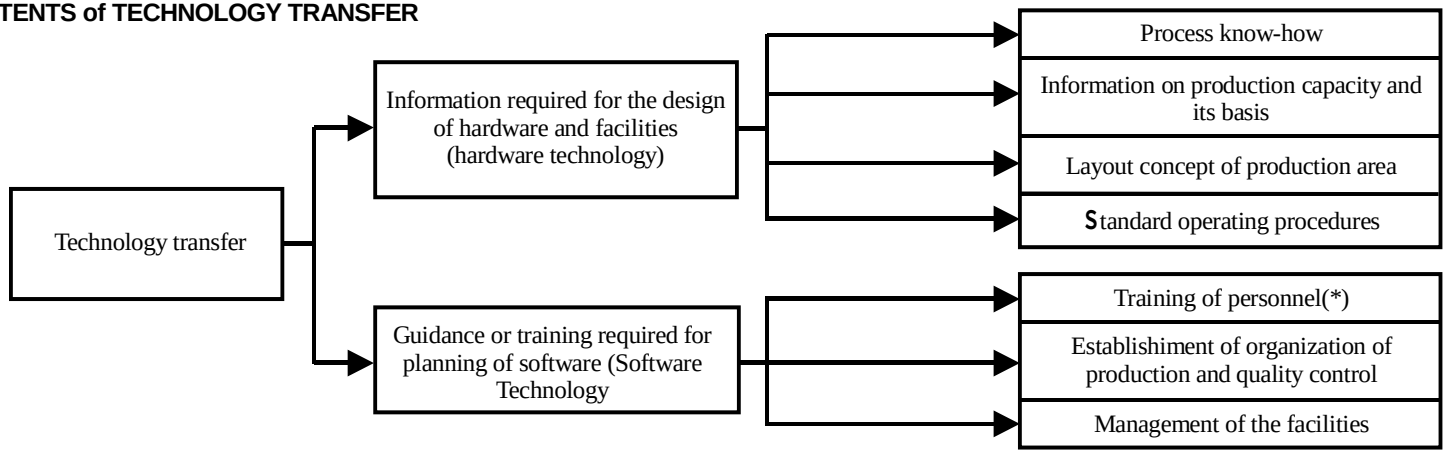
The main specifications for “Production Process”, “Production Environment”, “Utility service systems” were determined in the basic design for vaccine production facilities. At the same time, it is necessary to make plans to train and educate the staff of the facilities operator for the purpose of validation, and preparation for trial running and operation. It is essential to carry out these series of technology transfers in a well thought out manner. Contents of required technology transfer and the whole execution process of this project are described in the following diagram.

COMPLETE IMPLEMENTATION SCHEDULE FOR THE PROJECT



*Early involvement of the process licenser and co-work with the designer

CONTENTS of TECHNOLOGY TRANSFER



* Technology shall be transferred for both hardware and software components. Software transfer shall be in parallel with the execution of project implementation

Figure 2-1 Flow Chart of Technology Transfer and Project Implementation

2-2-2 Basic Design (Facilities Design/ Production Equipment Planning/Process Planning)

(1) Complete Frame of Cooperation Project (Analysis of Contents of Request)

1) Studies on Site and Contents of Final Request

Based on the initial request of January 2000, two on site studies were conducted and the final request from the Vietnamese side was confirmed. The summary of the final request is shown in Table 2-3 below.

Table 2-3 Contents of Final Request

Contents of Final Request	
Production Building	・Final Product Production Zone ・Bulk Production Zone ・Quality Control Zone ・necessary equipment for the above zones
Animal Laboratory	・Animal Laboratories ・necessary equipment for the above zones
Mechanical Building	・Mechanical Room (boilers, refrigeration machines, pumps, others), Transformer Room, Generator Room, others
Technology Transfer	・Measles Vaccine Production Technology ・Quality Control Technology for Measles vaccine ・GMP technology ・Validation technology ・Operation and maintenance technology of facilities and equipment
Others	・provision of stem cells (AIK-C strain) from Kitasato Institute ・provision of Bulk measles vaccine for 2 years after completion of the facilities

2) Analysis of Final Request Contents

The results of analysis of the contents of the final request are summarized in Table 2.4 below. (underlined portions indicate the differences between the request and the analysis results.)

Table 2-4 Results of Analysis of Request Contents

Contents of Final Request	Result of Analysis	Notes
(1) Request for Facility construction ・Production Building Final Product Production zone Bulk Production Zone Quality Control Zone ・Animal Laboratory ・Mechanical Building Mechanical Equipment room, Electrical room, Generator Room, Water Receiving room, others	(1) Request for Facility construction ・Production Building Final product Production zone Bulk Production Zone Quality Control Zone ・Animal Laboratory ・Mechanical Building Electrical and Mechanical equipment only for Mechanical Equipment room, Electrical room, Generator Room, Water Receiving room	* the structure and architectural portions of Mechanical building to be borne by Vietnamese Budget
(2) Request for Equipment ・minimum necessary equipment for the production of measles vaccine	(2) Request for Equipment ・minimum necessary equipment for the production of measles vaccine which are difficult to procure in Viet Nam	* Equipment which can be procured by the Vietnamese side to be borne by Vietnamese budget.
(3) Request for Technology Transfer ・measles vaccine production technology ・measles vaccine quality control technology ・GMP technology ・validation technology ・operation & maintenance technology for facilities and equipment	(3) Request for Technology Transfer ・validation technology ・operation & maintenance technology for facilities and equipment (to be conducted as Soft Component portion)	* Other technology transfers to be discussed in the future between Japan, Viet Nam and WHO.
(4) Others ・provision of Stem Virus (AIK-C strain) from Kitasato Institute. ・provision of measles bulk for 2 years after completion of facilities	(4) Others ・out of scope of Cooperation	*To be implemented under Vietnamese budget based on technology transfer agreement between POLIOVAC and Kitasato Institute.

(2) Site Plan

The main street is Doan Ket Street on the western side of the site. The main access to the site is through the main gate facing onto the street. Of the three main facilities to be constructed under the Project, the Production Building and Mechanical Building are located in line on the northern side of the central yard and the Animal Laboratory is placed at the back of the central yard entered from the main gate. The Administration Building, Canteen and Parking Garage are located in line on the southern side.

The elevation of the site is slightly higher on the east and gradually slopes to the west to obtain surface drainage. The sewer main is located under Doan Ket Street. The sewage treatment tank of the facilities is located at the northwest corner of the site near to the sewage mains.

Main Entrance (from West)

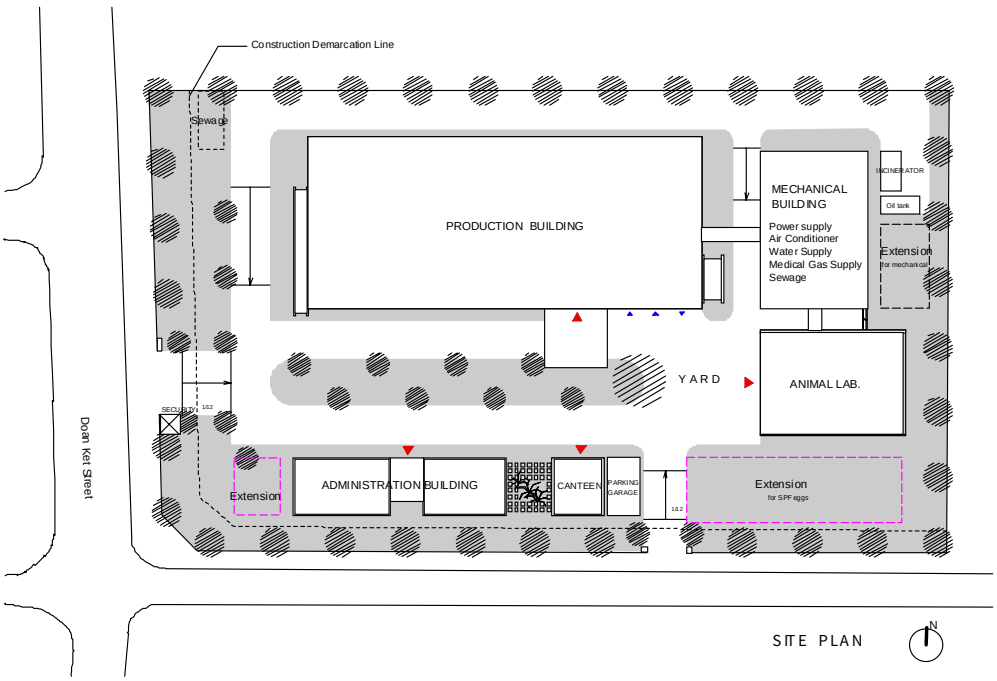


Figure 2-2 Site Plan

(3) Architectural Plan

1) Facility Components

The facilities of the Project are composed of the following components:

Table 2-5 Summary of the Project Facilities

Building Name, Floor	Facilities
Production Building (first floor)	Final product Production Zone, Receiving, Shipping & Storage, Water Processing Room, Air Conditioning Room
Production Building (second floor)	Bulk Production Zone(cell culture, virus culture, medium preparation), Quality Control Zone
Animal Laboratory (first floor)	Animal test laboratories, Washing Rooms
Animal Laboratory (second floor)	Air conditioning Room
Mechanical Building	Equipment for Boiler Room, Mechanical Equipment Room, Pump Room, Electrical Room, Generator Room,

*The structure and architectural portions of the Mechanical Building are to be borne by Vietnamese budget.

2) Determination of Facility Capacity and Dimensions

The capacity and dimensions of the Project facilities are determined based on annual measles vaccine production of 7.6 million doses. The determination of the capacity for each zone is shown below.

(Final product Production Zone)

Production capacity of one freeze-dryer machine is 30,000 vials at maximum and the time for one cycle of operation requires approximately 1 week. Considering the time required for cleaning and preparation, one cycle of operation will take approximately two weeks. This determines the whole production capacity and schedule of the entire facilities. In order to produce 7.5 million doses annually, there must be 25 cycles of freeze-dry operations in a year. This means that the freeze-dryer is working 25 X 2 weeks equal to 50 weeks, or almost in continuous operation throughout the year.

(Bulk Production Zone)

As producing one lot of Bulk takes about one month from the incoming of SPF eggs, in order to maintain the freeze-drying operation schedule, the capacity of Bulk production line should have at least the volume for two lots.

(Quality Control Zone)

Quality Control Zone should have the size and functions to enable the carrying out of all required tests at each step of vaccine production.

(Animal Laboratory)

Animal Test Zone should have spaces sufficient to accommodate the testing functions for the required number of mice, guinea pigs and rabbits. The required number of test specimens have been determined after consultations with Kitasato Institute, to be approximately, 1000 mice, 120 guinea pigs and 20 rabbits.

The following table enumerates the required rooms and their size based on each process and procedure, as has been determined after consultations with Kitasato Institute and POLIOVAC concerning production environment.

Table 2-6 Production Facility

Production Building

Zone/ Section	Name of rooms	Floor area (m^2)	Note
Final Product Production Zone	Washing room(2)	68.5	Autoclaves, dry ovens included
	Depacking room(1)	38.8	
	Vial Storage room	20.4	3.45m X 5.93m
	Vial Washing room & Sterilization room	43.1	12.0m X 4.25m
	Anteroom(4)	23.5	
	Clean room(5)	8.6	3.2m X 2.7m
	Filling Line room	60.4	9.1m X 7.2m
	Capping room	15.2	4.0m X 4.2m
	Inspection room	43.8	for 9 to 12 persons
	Record room	14.3	for 4 persons
	Freeze-drying room	71.9	9.1m X 7.9m
	Freezer room(1)	32.6	6.8m X 5.3m, Deposited for 3 months
	Cold room(3)	32.6	6.8m X 5.3m, Deposited for 3 months
	Anteroom(3)	3.7	Dumbwaiter included
	Pass Room	13.5	4 rooms
	Changing room	49.1	2 rooms for gowning & degowning
	Subtotal	540.0	
Packing & Depacking Zone	Anteroom(2)	11.4	5.6m X 2.1m
	Freezer room(2)	20.5	4.4m X 4.6m
	Cold room(5)	20.2	4.4m X 4.5m,
	Storage(7)	52.2	5.7m X 9.2m
	Sampling room	9.1	4.5m X 2.0m
	Packaging room	50.4	4.2m X 13.7m
	Depacking room(1)	13.3	5.3m X 2.5m
	Waste Shipping room	14.4	5.0m X 2.9m
	Anteroom(6)	5.5	1.9m X 2.9m
	SPF Eggs Receiving room	6.9	2.3m X 3.0m
	Pass Room	12.0	2 rooms
	Subtotal	215.9	
Bulk Production / Cell Culture Zone	Incubator room (SPF eggs)	7.4	
	Disinfection room	9.7	2.8m X 4.17m
	Cutting room	14.1	3.4m X 4.17m
	Weight Equipment room	11.5	3.92m X 3.5m
	Storage(1)	7.7	3.9m X 1.9m
	Media Preparation room	13.7	3.9m X 3.9m
	Sterile Filtration room	20.3	5.6m X3.6m
	Anteroom(2)	50.4	3.9m X 1.8m
	Storage(3)	7.1	1.5m X 3.2m
	Clean room(1)	21.8	Pass box included
	Clean room(2)	18.6	Pass box included
	Incubation room(1)	11.8	2.4m X 4.9m
	Centrifugation & Observation room	13.3	3.92m X 3.7m
	Storage(2)	5.3	
	Refrigerator room(1)	15.8	3.6m X 4.4m
	Cold room(1)	8.5	2.7m X 3.2m
	Pass Room	17.5	7 rooms
	Changing room	54.6	3 rooms included gowning/degowning
	Subtotal	309.1	

Zone/ Section	Name of rooms	Floor area (m^2)	Note
Washing Area	Washing room(0,1)	99.4	Autoclave/ Dry oven included
	Storage (6)	17.7	Drying area included
	Cleaning room	13.7	2.5m X 5.3m
	Subtotal	130.8	
Bulk Production/ Virus Culture Zone	Clean room(4)	28.0	Pass box included
	Storage (5)	9.7	2.6m X 3.7m
	Clean room(3)	16.5	3.6m X 4.9m
	Anteroom(2)	34.4	
	Observation room(2)	9.6	3.1m X 3.1m
	Cold room(2)	9.3	3.1m X 3.0m
	Incubation room(3)	8.3	3.1m X 2.7m
	Freezing room	7.0	
	Refrigerator room(3)	14.9	3.1m X 4.8m
	Thawing room	7.7	Dumbwaiter included
	Storage(5)	9.7	2.7m X 3.7m
	Pass Room	4.8	2 rooms
	Changing room	30.9	2 rooms, gowning/degowning, AL included
	Subtotal	190.8	
Quality Control Zone	Washing room(3)	24.6	Autoclaves, Dry ovens included
	Observation Area	23.6	2.6m X 9.7m
	Clean room(6)	12.8	3.2m X 4.0m
	Clean room(7)	17.9	3.0m X 6.0m
	Incubation room(3)	6.3	3.0m X 2.1m
	Incubator room(2)	5.4	3.0m X 1.8m
	Refrigerator room(4)	13.9	3.0m X 4.6m
	Clean room(8)	19.9	Pass box included
	Anteroom(7)	2.5	1.9m X 1.3m
	Preparation room(3)	6.5	Pass box included
	BSL2 + Incubator room(3)	9.7	3.75m X 2.6m
	Anteroom(8)	1.5	1.1m X 1.4m
	Chemical Test room	31.5	Including measuring room
	Moisture Content Test room	10.9	4.1m X 3.0m
	Immunological Test room + Laboratory	11.6	4.1m X 3.0m
	Cold room	4.8	2.0m X 2.4m
	Storage(8)	15.9	4.7m X 3.4m
	Pass Room	4.5	One room
	Changing room	29.0	2 rooms, gowning/degowning
	Subtotal	252.8	
Administration	Changing room	56.1	2 rooms for 60 persons, with shower
	Documents room	46.0	2 rooms
	Meeting room	26.0	2 rooms for 8 persons
	Record room	24.8	6.6m X 3.8m
	Subtotal	152.9	
Service	Air Conditioning rooms etc.	509.9	Including EPS
	Pantry	4.8	3.2m X 1.5m
	SK	2.3	2.2m X 1.1m
	Security room	8.9	3.0m X 3.0m
	Subtotal	525.9	
Common	Entrance Hall	30.6	
	WC	48.2	1F: 21.5㎡, 2F: 26.7㎡
	Corridor etc.	719.0	
	Subtotal	797.8	
Total		3116.0	

Animal Laboratory

Zone/ Section	Name of rooms	Floor area (m^2)	Note
Animal Laboratory	Storage(1)	10.4	Animal food
	Washing room	36.5	1Autoclave included
	Storage(2)	6.3	2.1m X 3.0m
	Material In	4.4	2.4m X 1.85m
	Material Out	4.4	2.4m X 1.85m
	Changing room	11.5	2 rooms included gowning/degowning
	Quarantine room	11.5	2.4m X 2.4m X 2 rooms
	Autopsy room	9.5	2.4m X 2.0m X 2 rooms
	Rabbits Test room	5.4	2.7m X 2.0m
	Guinea Pigs Test room	6.7	2.8m X 2.4m
	Inoculation room	23.6	4 rooms
	Mice Test room	12.4	2rooms
	Storage	5.8	2 rooms for clean area
	Clean Corridor	22.7	2 rooms
	Dirty Corridor	32.9	2 rooms
	Document room	12.7	for 5 persons
	Subtotal	216.7	
Service	Air Conditioning rooms etc.	66.1	
	Subtotal	66.1	
Common	Changing room	17.1	2 rooms including shower rooms
	WC	6.1	Separate Men & Women
	Corridor etc.	52.3	
	Subtotal	75.5	
Total		358.3	

Mechanical Building

Zone/ Section	Name of rooms	Floor area (m^2)	Note
Service	Workshop	23.8	
	Machine rooms etc.	460.9	
	Subtotal	484.7	
Total		484.7	

Grand Total

Building name	Floor	Area (sqm)
Production Building	1st Floor	1,591
	2nd Floor	1,525
	Sum	3,116
Animal Laboratory	1st Floor	292
	AC Floor	66
	Sum	358
Mechanical Building	1st Floor	484
	Sum	484
Total	Sum	3,958

3) Building Design

i. Floor Plans: (Refer to Floor Plan Drawings)

The production building is composed of 4 main zones, Final product Production Zone, Packing/Depacking Zone, Bulk Production Zone and Quality Control Zone. On the first floor of the Production Building, the Final product Production Zone is separated from Packing/Depacking/Storage Zone by locating the Changing rooms in-between. On the second floor, Bulk Production Zone is clearly separated from Quality Control Zone by positioning the common spaces including an elevator shaft, lobby and restrooms in between. In particular, since Quality Control Zone requires prevention of personnel of other sections from entering without proper clearance, an identity checking system is provided at the entrance to the Quality Control zone to control uncertified entry. The Bulk Production Zone has the Washing rooms placed in the center, facilitating the common use of washing activities from both cell culture and medium culture areas.

In the Animal Laboratory, the circulation lines and spaces of the mouse test area and guinea pig/rabbit test area are completely separated to prevent cross-contamination. A one way circulation for each area is planned, to reflect the consideration against contagion.

(Zoning and Gowning Rules)

The main zoning and gowning rules which are necessary to maintain the required cleanliness of each process and zone are described below. The architectural design and building systems design are based on the rules.

・Zoning

Zoning is based on the characteristics of each production process in compliance with WHO-GMP. Each production process is regarded as an aseptic process. The basic rules for aseptic areas are applied to the rooms for Final product Production Zone, Bulk Production Zone (cell culture and medium culture sections), Quality Control Zone in the Production Building and for the rooms in the Animal Laboratory.

Table 2-7 Class of Cleanliness

Classification	Maximum Permitted Number of Particle per m^3		Maximum permitted number of microbes CFU/m^3	Note
	0.5-5 μm	5 μm≦		
Grade A	3,500	0	Less than 1	Rooms where aseptic tests are conducted and rooms where final bulk is handled in exposed condition. 1F: Laminar Booths in Filling Line Rm., Clean Rm. (5), etc. 2F: inside Cabinet in Clean Rm. (8)
Grade B	3,500	0	5	Areas surrounding Grade A areas. 1F: Filling Line Rm., Clean Rm. (5) etc. 2F: Clean Rm. (8), etc.
Grade C	350,000	2,000	100	Rooms in which bulk suspension is exposed or sterilized materials are exposed. 2F: Clean Rm. (1), (2), (3), (4) and Sterile Filtration Rm., etc.
Grade D	3,500,000	20,000	500	Rooms in which pre-sterilized materials are exposed or sterilized materials are stored. 1F: Washing Rm. (2), etc. 2F: Cold room, Media Preparation room, etc.
Normal Zone	-	-	-	Rooms that do not require high sterility (production support rooms, etc.) 1F: Vial Storage Rm., Depacking Rm., etc. 2F: Incubator Rm. (1), Washing Rm. (1), Record Rm., etc.

* Note: Maximum permissible numbers indicated above are those counted under “at rest” conditions.

・Gowning Rules

・Primary Gowning: Immediately after entering Production Building, changing to white uniforms and indoor shoes are done in the changing rooms

・Grade D: Protection gowning with cap is required along with shoes change.

・Grade C: Dust free gowning with dust free hood and mask is required along with shoes change.

・Grade B: Dust free gowning with dust free hood, mask, and goggles is required along with changing shoes and socks to boots and clean socks.

ii. Elevation Design

The Project facilities contains many rooms which require strict control of air conditioned environment. External walls are designed with minimum window openings in order to lessen air conditioning loads. Walls on the second floor and above are finished with ceramic tiles or wash gravel finish, which require relatively less maintenance. Walls on the lower levels, which can be easily reached, are finished with easily maintained painting.

Roof construction is made of sloped concrete slabs clad with finishing materials and external thermal insulation, to counter the severe climate conditions of the area.

iii. Section Design

Production facilities have many rooms requiring high cleanliness of air and the ceiling plenum should be high enough to contain A/C ducts and other piping. Maintenance of the ducts and piping are also required and the sectional design will take these requirements into consideration.

Access routes to the ceiling plenum on first and second floors are secured through external stairs so that maintenance staff can have direct external access.

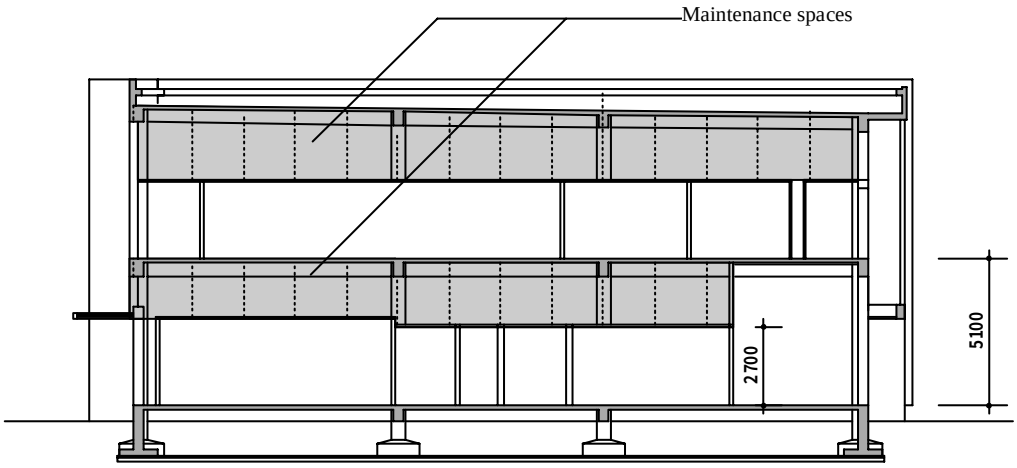


Figure 2-3 Sectional Drawing

(4) Structural Plan

1) Structural Planning

i. Production Building

The building plan is rectangular, with dimensions of approximately 60 m x 25 m. Major spanning is 6 m to 8 m in the longitudinal and 7.2 m to 9 m in the transversal direction, appropriate for the production process. It is a two-story structure with floor heights of 5.1m for both floors. Structural type is a reinforced concrete frame structure, commonly found in Viet Nam. Bearing wall system is not common in Viet Nam and the frame structure constituted by the columns and beams will resist the lateral forces caused by seismic activities.

ii. Animal Laboratory

The building plan is a single story structure of rectangular shape with dimensions of approximately 12 m x 18 m. The building is partially two stories, with the mechanical systems housed among the roof structure. The building is a reinforced concrete frame structure like the Production Building.

2) Foundation Design

i. Soil Conditions of Site

The project site is located on the flood plains of the Red River. The bearing soil layer for Production Building is the gravel and sand layer found at a depth of about 42 m. Soft clay overlies this layer from close to the surface to a depth of about 23 m.

According to laboratory soil tests, most of this clay layer shows characteristics of incomplete consolidation. Based on this test result it is assumed that settlement is occurring on the site at present. Furthermore, the result of plate loading tests at the surface level indicate bearing capacity of only 6 to 8 tons/m^2 which normally demands very careful studies prior to selecting direct foundation system for heavy building loads.

Accordingly in case of large and heavy buildings such as the Production Building, pile foundations are necessary. As has been noted above, the site is undergoing consolidation of the soil and it is calculated that maximum settlement of 15 to 20 cm will occur. Small and lighter buildings, which are designed for direct foundations, must be designed with protective measures to prevent damage from differential settlement in and outside of the building.

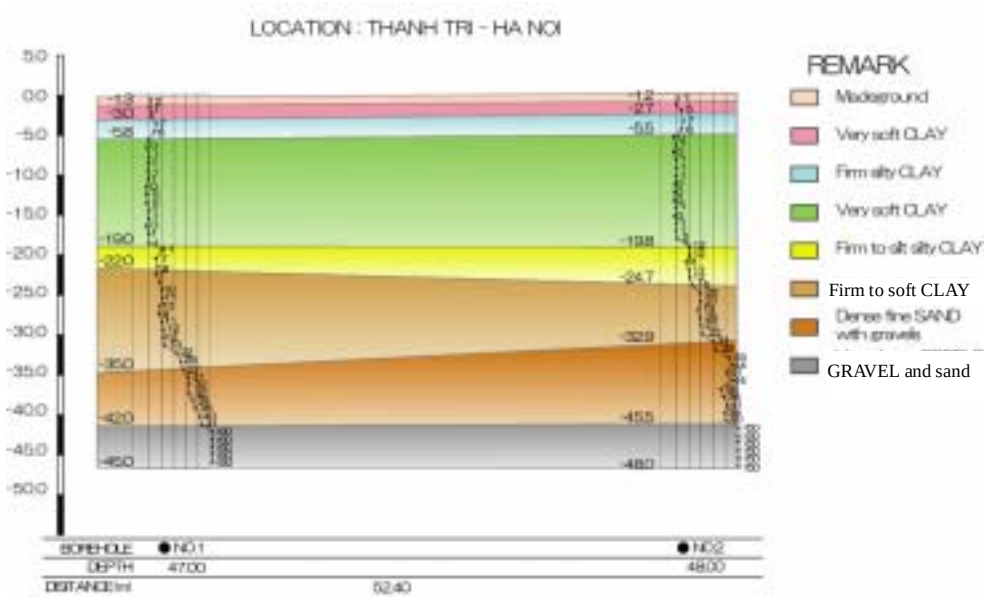


Figure 2-4 Geotechnical Profile

ii. Production Building

This building has many rooms containing heavy production equipment. There is a high possibility of differential settlement in case direct foundations are selected. Since disturbance to production is considered to be severe in case of uneven settlement of floors, this building is designed with bearing pile foundations.

iii. Animal Laboratory

Considering the small size and lightness of this single story building with symmetric shape, there is less possibility of uneven settlement. It has been decided to select direct foundations for this building. However careful design to counter effects of ongoing settlement at connections to the external works as well as jointworks of plumbing, et cetera are required.

3) Basic Policy for Structural Design

Basic policy for the structural design for this Project is summarized below:

- External forces and design loads are decided according to the local meteorological data, geography, geotechnical data and use of buildings.
- Stress and shear strength of materials will be based on Building Code of Viet Nam. However design strengths are adjusted with consideration for quality of materials.
- Stress analysis and sectional calculations of frames will be carried out according to Building Code of Viet Nam along with structural codes of Japanese Institute of Architectural and Building Science.

4) Design Loads and External/Forces

Design loads and external forces are principally calculated following Building Code of Viet Nam.

i. Dead Load: The dead loads will be calculated respective to the weight of materials in each part of the buildings.

ii. Live Loads: Live loads are calculated with reference to TCVN2737 "Live Loads and Impacts- Design Standards" of Building Code of Viet Nam. Design standards in the Japanese Building Code will be adopted when necessary. Standard load values are shown in Table 2-8.

Table 2-8 Standard Live Load

Name of rooms	Live loads (N/mm^2)
General offices, Corridors	1,800
Workshops, Laboratories	2,900
Mechanical system rooms	7,800
Roof	1,000

iii. Wind Loads

Wind loads are calculated following TCVN2737 of Building Code of Viet Nam, which states the standard wind velocity for each region. Hanoi City belongs to II_B region, where the standard wind pressure is 95 daN/m^2 for structural design.

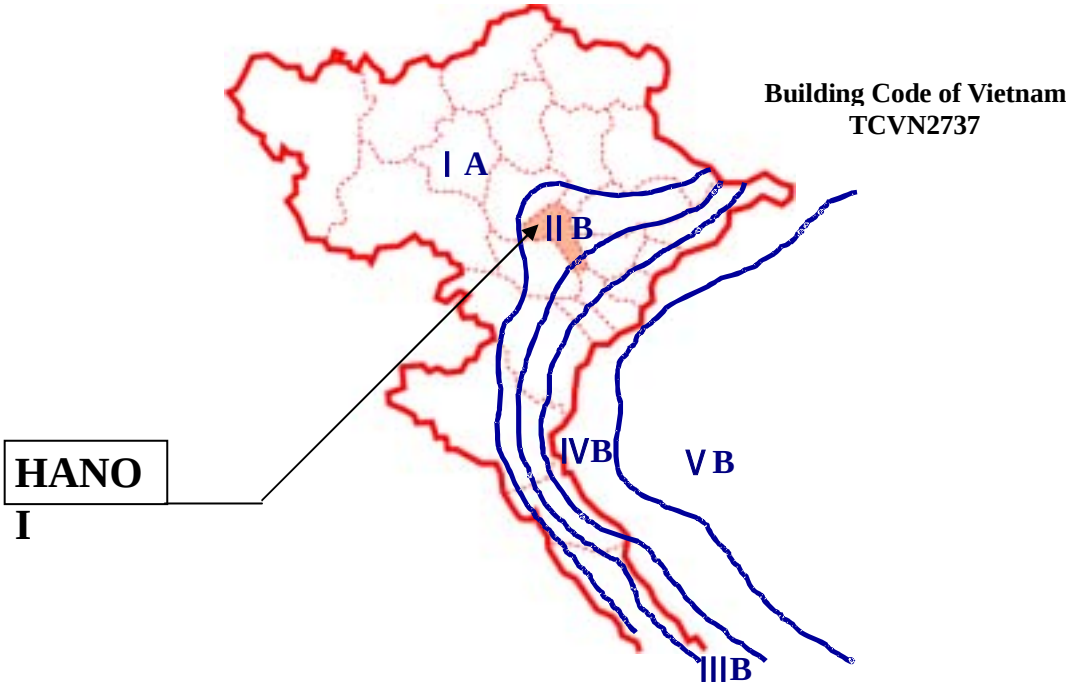


Figure 2-5 Wind Pressure Zoning in Northern Viet Nam

iv. Seismic Loads

Almost no earthquake occurrence over magnitude 6 in Richter scale has been recorded in the vicinity of Hanoi. Magnitude 6 will be the design strength of the earthquake. The surface acceleration of a magnitude 6 earthquake is roughly equivalent to a quarter of the design acceleration force in the Japanese Seismic Design Law. Therefore, one fourth of seismic force of Japanese standard is chosen for the structural design of the Project facilities.

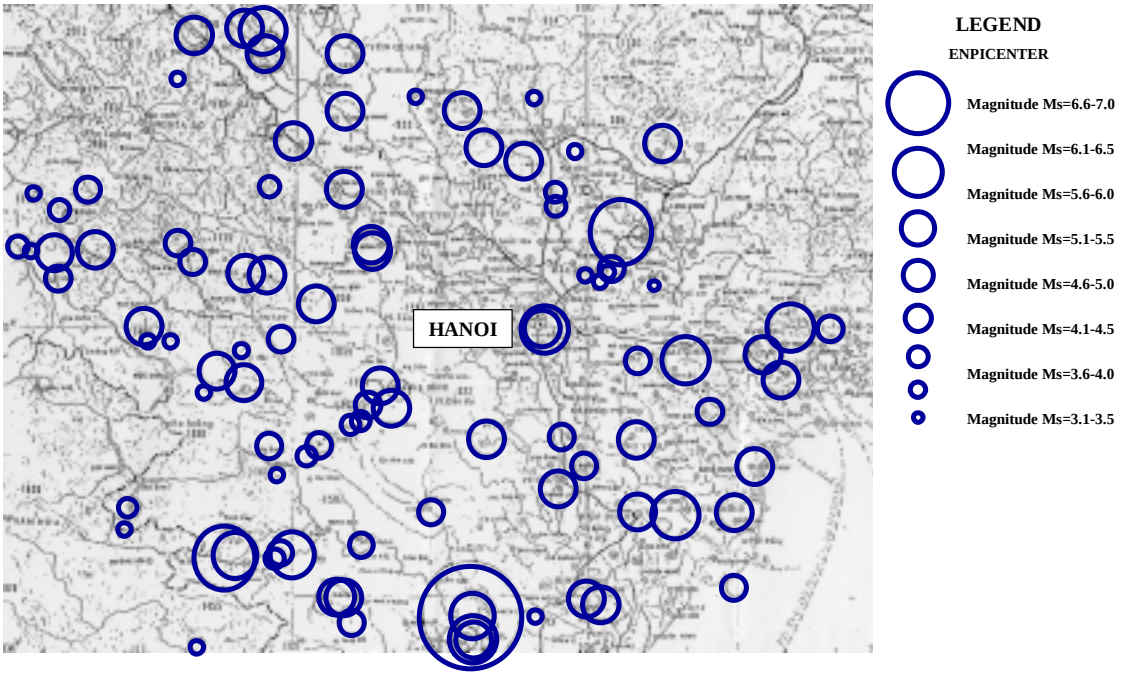


Figure 2-6 Record of Earthquakes in the Vicinity of Hanoi

5) Materials to be used in the Project and their strengths

Concrete: Normal concrete with standard design strength of Fc = 24 N/mm^2

Reinforcing bars:

Locally available deformed bars with specifications in accordance with JIS G 3112 are selected for the Project. Two types with design strengths of SD295: fy = 295 N/mm^2 and SD345: fy = 345 N/mm^2 are selected.

(5) Building Systems Plan

1) Electrical System Plan

① Electrical Power Supply Facilities

Electrical power will be supplied to the electrical room in Mechanical Building from the nearest substation of Hanoi Power Company (HPC) by a single circuit three phase/three wire 6.3 kV line.

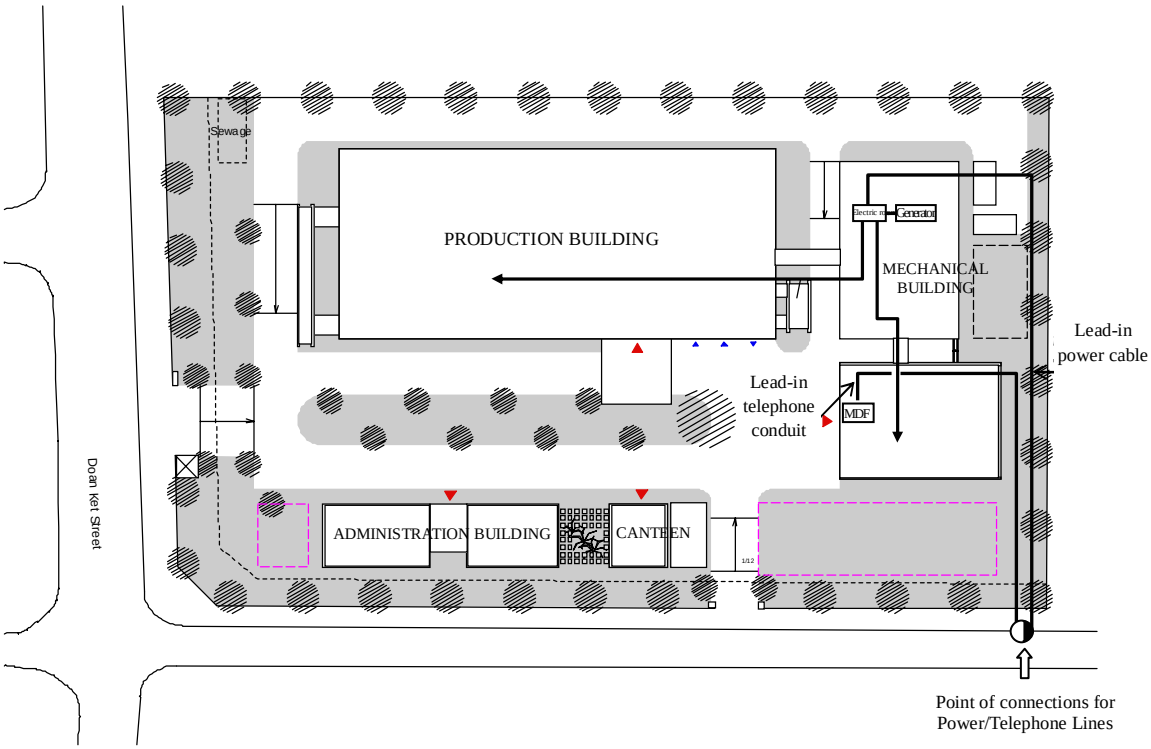


Figure 2-7 Routing Plan for Utilities Mains

Required amount of electrical power is estimated to be approximately 1,200 kVA. The necessary transformers and switchboards are to be installed to distribute power to each demand load. The calculation for required transformer capacity includes demand loads for Administration Building, Canteen and other ancillary buildings to be constructed by Vietnamese budget as well as the planned addition of a freeze-dryer unit. Distribution system will be 3-phase 4 wire 380/220 V in accordance with standard distribution voltage in Hanoi.

As the result of field surveys, voltage fluctuations of commercial power is expected to range from +5% to -10%. Each piece of equipment will be provided with an automatic voltage regulator (AVR) for protection from the fluctuations.

Power failure in Hanoi area is reported to occur several times monthly, including planned blackouts, with a maximum half-day duration. In order to maintain the continuous operation of freeze-dryer, refrigerators, air handling units and other critical equipment during power failure, diesel generators will be installed as the source of emergency power. It has been confirmed that quality of product is not affected by short time stoppage of freeze-dryer due to power failure of less than 10 to 20 minutes duration and no installation of uninterrupted power system (UPS) is considered necessary. Generators and surrounding structures will be furnished with adequate noise insulation and vibration absorbers in consideration of the surrounding environmental conditions.

Underground fuel tank, to be used in common with boilers, with capacity for one day operation of generators are provided, allowing long duration of operation.

② Lighting Fixture and Power Sockets

Design luminance is set at 60 to 70% of Japanese Industrial Standard requirement, considering the present conditions in Viet Nam. Lighting fixtures are mostly fluorescent lights due to their higher lighting efficiency. Lighting fixtures in the clean area should have suitable performance to respective cleanliness requirement of each room.

Power sockets are earthed, two round pin type or flat parallel pin type normally used in Hanoi. Power lines and sockets in clean rooms are designed with appropriate dust proofing sealents.

Design luminance in major rooms:

Working area	approx. 400 Lx
Common area	approx. 150 Lx

Lighting fixture:

Grade A to C:	Ceiling recessed type with cover for clean rooms
Grade D:	Ceiling mounted type for clean rooms
Normal areas:	Ceiling recessed type with open bottoms

③ Lightning Rods, Conductors and Grounding System

To protect the facilities from lightning, lightning rods and rooftop conductors will be installed. Grounding system will be installed and connected to production equipment, electrical equipment and communication appliance as required.

④ Telephone System

A new telephone line will be brought in from existing overhead main cable of Hanoi City Telecom to a MDF to be located in the office in the Animal Laboratory. The capacity of the incoming cable will be at least 30 external lines including considerations for future demand increase. As the required number of lines is 20 external connections and 100 internal extension lines, the necessary telephone exchange boards (PABX) are provided.

The lead-in installation costs incurred from all connection works upto the MDF will be borne by Vietnamese budget.

⑤ Paging System

Main unit of paging system will be installed in the office in the Administration Building. This system will make it possible to page all staff in the facilities and make emergency announcements in case of fire, etc., through centrally controlled system. All equipment related to paging system installed in clean rooms will be airtight to maintain cleanliness. A remote microphone will be installed in the office in the Animal Laboratory.

⑥ Interphone System

Simple type of interphone system will be provided for the purpose of internal communication in the facilities. Reception interphone for nighttime use will be installed between gate and office in Administration Building. All interphones installed in clean rooms are designed to prevent dust accumulation.

⑦ Automatic Fire Alarm System

According to Vietnamese fire codes, automatic fire alarm system must be installed for the purpose of early detection of fire and prevention of spread of damage. Gas detector will be provided whereever flammable gas is used. Central control room in Mechanical Building will have surveillance panel to detect fire alarm. Fire alarm equipment in clean room will have high air-tightness to maintain cleanliness.

Minimum necessary fire protection based on Japanese fire code will be applied to any areas of fire protection/prevention not covered by the Vietnamese fire code.

2) Mechanical Building Systems Plan

① Water Supply System

City water will be brought in from the new city water main pipe to be installed under the adjacent Doan Ket Street. Emergency water supply is planned to be taken from wells. The volume of water supply required for the Project is estimated to be approximately 90 m^3/day.

Water supply systems in Production Building consist of two systems, namely General Water Supply System and Production Water Supply System. The source of water is principally city water. Incoming city water is brought into the water reservoir in the underground pit of the Mechanical Building, then pumped up to the elevated water tank and distributed to each use point of General Water Supply System such as pantries, lavatories, hand wash basin, etc. In the Production Water System, the water is treated in the primary treatment plant in the Mechanical Building. Next, the water is sent by booster pumps to the Production Water Supply Equipment, where it is given secondary treatment. The secondary treated water is sent to WFI water, UF water or pure steam process equipment in Production Building.

It is noted that any well digging and required treatment of the well water will be the responsibility of the Vietnamese side.

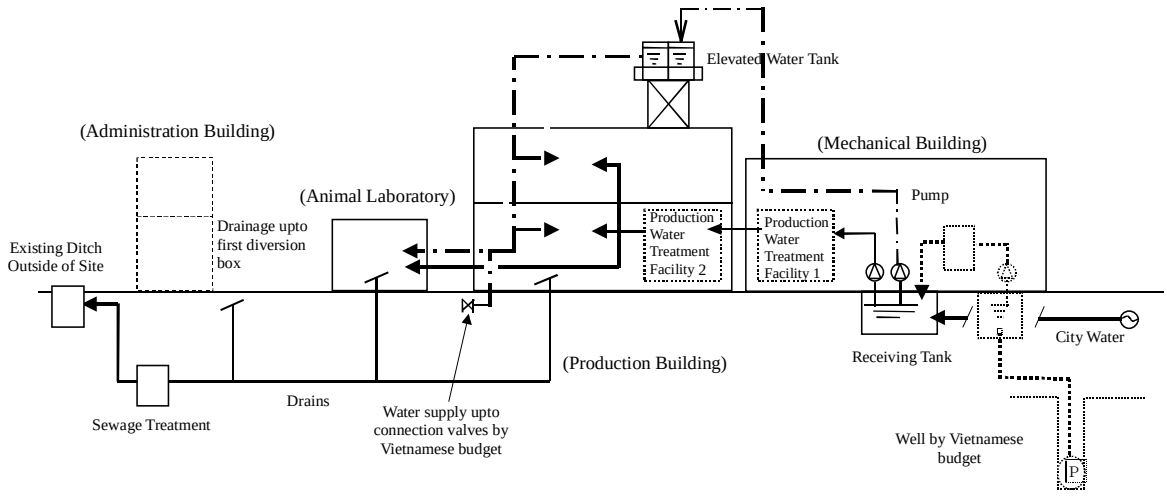


Figure 2-8 Diagram of Water Supply System

② Sewage and Drainage System

Sewage and general wastewater from lavatories, wash basins and shower rooms is treated in the sewage tank and discharged to the existing neighboring ditch. Discharged water will be in compliance with relevant Vietnamese environmental code and have a target Biological Oxygen Demand (BOD) of 20 ppm.

A neutralization tank will be provided to treat chemically contaminated sewage discharged from production or testing processes and a sterilization tank will be provided to treat waste water from the animal laboratories, after which the waste water will be piped to the regular septic tank to receive final treatment. Organic solvents will be collected into plastic tanks and taken out of site for treatment by designated contractors.

Rainwater will be collected through on-site drainage system and discharged to the existing open ditch along the street.

③ Hot Water System

Almost no hot water is used in Production Process or Quality Control Operations. Shower rooms, pantries and others in Normal Zone will be supplied with hot water from individual supply systems.

④ Sanitary Equipment

Type of sanitary furnishings will be selected from either Western or Vietnamese style. From the viewpoint of maintenance after completion, local availability is the first priority in selection.

⑤ Propane Gas Supply System

Vaccine production does not require a large amount of gas. A propane gas system using individual propane gas cylinders is selected for the Project.

⑥ Fire Fighting System

Fire fighting system in the Project should be in compliance with Vietnamese Fire Code. The Project facilities are provided with the following facilities.

Interior Fire Hydrants:	Required points in all buildings.
Exterior Fire Hydrants:	Three exterior hydrants.
Fire Extinguishers:	Required points in all buildings
Fire Cistern:	One underground tank (to be constructed by Vietnamese side)

⑦ Medical Gas System

Only compressed air is provided for the Project. Compressed air will be central pipe type from considerations for safety, operability and ease of maintenance.

Individual equipment requiring medical gases (nitrogen gas, others) will have individual supply systems.

⑧ Incinerator

In the Study it was found that Hanoi Environmental Agency does not accept test animal remains as part of ordinary waste. These remains must be either collected by a designated contractor or incinerated.

An incinerator is to be provided on site as part of Vietnamese budget construction items. Dioxin generation will be prevented by strictly enforcing separate collection of differing categories of combustibles.

⑨ Air Conditioning System

i. Air Conditioning Parameters

The air conditioning system is designed under the following parameters.

Exterior Air Conditions	Summer		Winter	
	temperature	humidity	temperature	humidity
exterior	35°C	60%	10°C	80%

Interior Air conditions	Summer		Winter	
	temperature	humidity	temperature	humidity
Production Building (Clean rooms)	24±2°C	50±15%	22±2°C	50±15%
Animal Laboratory (clean rooms)	24±2°C	50±15%	22±2°C	50±15%
General rooms	26±2°C	-	24±2°C	-
Moisture content room	24±2°C	Less than 30%	22±2°C	Less than 30%
Incubation room(1)	37.5±0.5°C		37.5±0.5°C	
Incubation room(2)	32+0.5°C		32+0.5°C	
Incubation room(3)	37+0.5°C		37+0.5°C	

ii. Heating and Cooling Facilities

Heating facilities:

Steam is required for the use of autoclaves, distilled water production and re-heating in air conditioning system. Steam boilers of diesel oil type will be installed. Several units will be installed as back up for maintenance and breakdowns.

Cooling facilities:

Refrigeration machines will be installed mainly for air conditioning. Back up units will be installed as same as for heating facilities. Local operation and maintenance practice in Viet Nam will be the criteria for selecting easily operated and maintained cooling units.

iii. Zoning of Air Conditioning

The facilities in this project must be in compliance with WHO guidelines. The main points of WHO GMP code are described below:

- Clear zoning between clean areas and normal areas
- Prevention of cross-contamination
- Securing the specific grades of air cleanliness.

iv. Air-conditioning Zoning

a) Clean Rooms

Air cleanliness of clean rooms is dependent on performance of filters, ventilation cycles, airflows and distribution of room pressure. The following items are specified in the design to achieve the required cleanliness of respective rooms.

Item	Specification
Filter	Combination of prefilters, mid-performance filters and HEPA filters
Ventilation rate:	Recirculating air volume of 40 times to 20 times room volume per hour according to room grade
Air cleanliness:	The particle and microbe numbers permitted for each grade are as described in Table 2-7.
Airflow Patterns	Turbulent type airflow
Air Pressure differentials	Basically, 1 mmAq pressure differential will be designed between differing grades
Temperature & humidity control	Temperature & humidity is measured for each room or zone for air conditioning control. Electrical reheaters are provided as needed.

Air conditioning System in Production Building Clean rooms

The air conditioning system for the clean rooms in the production building are provided with circulating air conditioning system. The exhaust fans are selected to provide exterior air intake equivalent to 3~5 times per hour turnover capacity, in order to quickly reduce interior formalin density after fumigation with formalin.

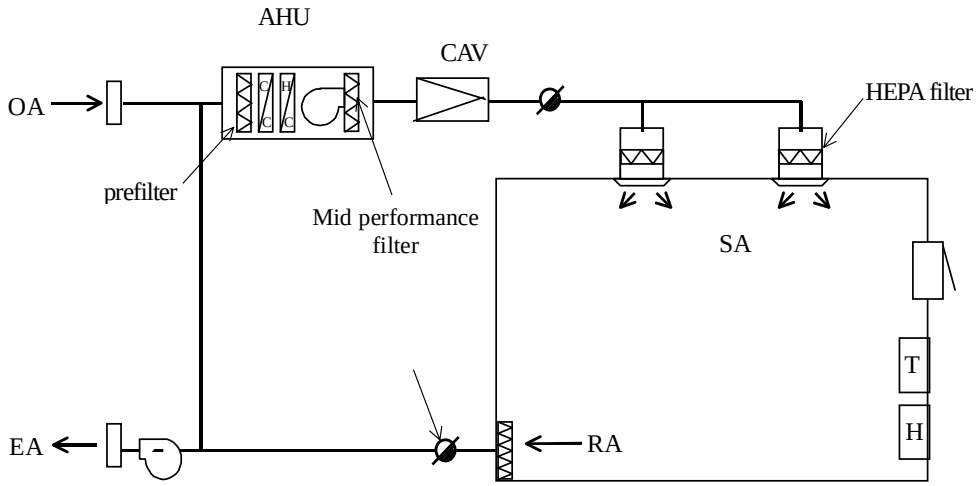


Figure 2-9 Air Conditioning Diagram for Clean Room in Production Building

Air conditioning System in Animal laboratory Clean rooms

Complete turnover ventilation system is used and no air will be recirculated in the air conditioning systems for Animal Laboratory. Exhaust air will be released after treatment with deodorant filter to reduce odor pollution to neighboring areas.

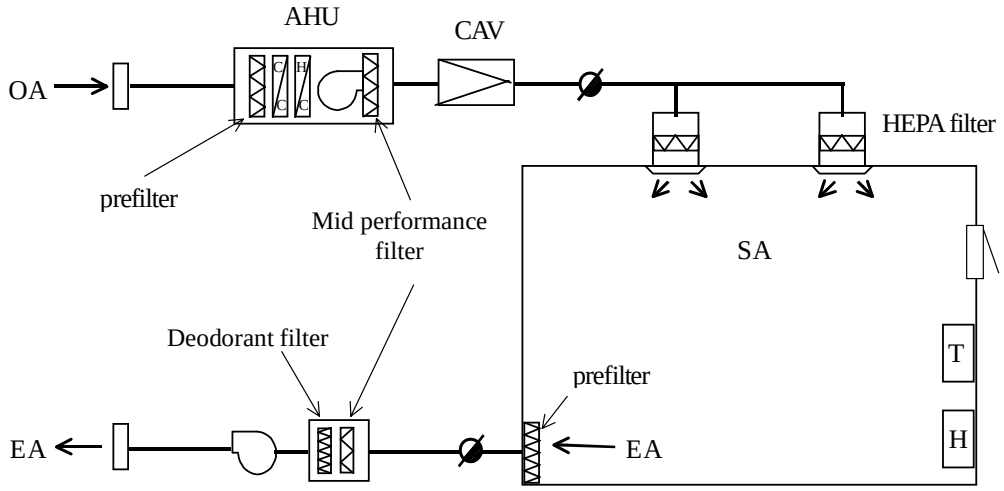


Figure 2-10 Air Conditioning Diagram for Clean Room in Animal Laboratory

b) Air-conditioning in Normal rooms

Rooms and areas other than the clean rooms are provided mainly with room cooling. Room temperature is controlled by temperature in return ducts. Offices to be used under different working schedules are air-conditioned by air cooled package units.

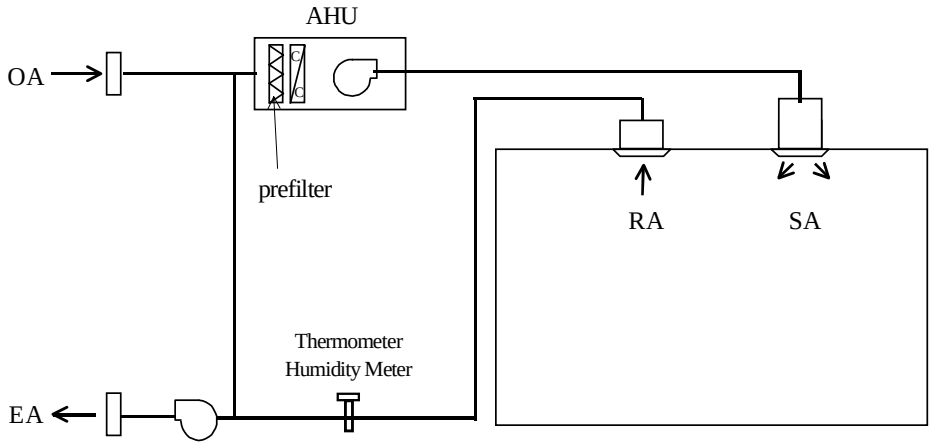


Figure 2-11 Air Conditioning Diagram for Normal Rooms

(6) Construction Material Plan

Materials which are durable and easily maintained and are normally used in Viet Nam are selected as the construction materials for the Project. The procurement of materials and equipment from Japan and third countries can not be precluded due to the special requirements of vaccine production facilities of the Project, but any material or equipment selected for use in the Project will be confirmed to be in compliance with Vietnamese codes and regulations. The following are the basic considerations for selecting materials for project buildings:

1) External Finish

i. Roofs

- Roofs are adequately sloped to achieve good drainage of rainwater during the rainy season.
- In case flat roofs are used, the concrete slabs will be designed with more than 1 in 75 slope, applied with reliable asphalt waterproofing and finished with high efficiency external thermal insulation materials.

ii. External Walls

Considering the requirements for maintenance, waterproofing and humidity resistance, paint finish over exposed concrete or mortar on concrete block walls are selected. Areas that cannot be easily maintained will be designed with relatively easily maintained tiles or wash gravel finish.

iii. Windows and Doors

Windows on exterior walls will be made of durable anodized aluminum. Entrance doors used by a large number of people will be made of stainless steel and other doors will be made of steel.

2) Interior Finish

i. Floors

Cleanliness and chemical resistance is the most important factors selection of floor finishes in the Project facilities. Epoxy resin coating is selected as main finish for its ease of cleaning and dust-free nature.

ii. Walls and Partitions

Main rooms on the first and second floors of the Production Building which require fumigation with formalin will be designed with walls of decorated silica-acid calcium boards or baked finished steel panels. Water sections such as lavatories, shower rooms and contaminated waste treatment rooms where contaminated matter may stick to walls or are often dirtied will be finished with porcelain tiles for easy maintenance.

iii. Ceilings

Ceilings of rooms requiring cleanliness (Grade B, C, and D) will have two types of finish. In rooms that require frequent maintenance in ceiling plenum, baked finished steel ceiling panels will be provided, to allow walking within the plenum. Rooms with relatively little in-plenum maintenance requirements will be provided with coated silicic-acid calcium panels with maintenance catwalks in the ceiling plenum. Both finishes will also be coated with material capable of withstanding formalin fumigation.

Ceilings will be finished with paint finished silicic-acid calcium boards for other rooms using water.

iv. Windows and Doors

Windows and doors in production areas will be anodized aluminum because of better anti-rust performance. In other normal rooms, aluminum windows and steel doors will be used. Selection of finishing materials and construction is summarized in Table 2-9 below.

Table 2-9 Finishing Materials and Construction Method

Portion of Building	Local Construction Method	Construction Method for the Project Building	Reasons for Selection
Roofs	Flat roofs (asphalt waterproofing)	Flat roofs with asphalt waterproofing & external thermal insulation.	Compatible with local construction method and easily maintained. High thermal resistance.
Exterior walls	Paint finish on cement mortar	Paint finish on cement mortar Ceramic Tiles Gravel Wash-out finish	Compatible with local construction method and local knowledge of maintenance. Relatively high durability and good maintenance performance.
Floors	Ceramic tiles	Epoxy resin coating finish	Easy to clean and joint-less finish reduces molds and dusts gathering. Good resistance to chemicals.
Interior walls and partitions	Ceramic tiles Paint finish	Coated silicic-acid calcium boards with sealed joints. Baked finish Steel panels w/ sealed joints	Easy to clean Good performance in reducing number of particles in the air. Durable against formalin fumigation
Ceiling	Paint finish Acoustical tiles	Factory painted steel sheets Factory made silicic-acid calcium boards Acoustical tiles	Durable material to allow walking & maintenance in ceiling plenum is required Good cleanliness performance in reducing number of particles in the air. Durable against formalin fumigation. Economical for normal use.
Doors and Windows	Anodized aluminum Steel Wood	Anodized Aluminum Steel Stainless steel	Compatible with local construction method, Stainless steel doors for busy entrance and places requiring both cleanliness and high durability

(7) Equipment Procurement Plan

1) Equipment Plan

The basic policy concerning equipment procurement plan is to provide the minimum necessary equipment to produce 7.5 million doses of measles vaccine annually. The production equipment that can be procured by Vietnamese funding is placed in the Vietnamese portion of the Project.

The Study Team held detailed discussions with the Vietnamese side on the requested equipment for each zone of the production facilities during the second Basic Design Study Mission and established the following priorities from A to E.

Priority A: Expensive and essential equipment for vaccine production, difficult to procure locally.

Priority B: Expensive and essential equipment for vaccine production, but locally procurable.

Priority C: Not very expensive, but essential equipment for vaccine production, difficult to procure locally.

Priority D: Not very expensive, but essential equipment for vaccine production, locally procurable.

Priority E: Not essential for vaccine production, but required for the implementation of the Project.

Following the final discussions with Vietnamese side, it was decided that items with priority rankings from Grade A to D are essential for production of vaccine and require highly reliable equipment. These items are to be basically procured under Japanese funding.

However, some items in priority ranking A (1item), B (3 items), C (4 items) and D (11 items) were decided to be procured by Vietnamese funding after discussion with concerned Japanese parties, since it was deemed possible for Vietnamese side to procure the items when appropriate technological guidance is provided.

As the results of the discussions on equipment procurement, final contents were determined as indicated in the following list of equipment.

Table 2-10 Equipment Procurement Analysis

Additional Items of Equipment
Laminar flow unit, Vacuum drying oven, Dispenser, Ultrasonic cleaner, Air velocity meter, All sinks, Constant temperature device immersion, Disinfection Tank, Sealers, Portable pump for waste liquids, Air samplers, Recorder

Eliminated items from the list of original Vietnamese request on the ground that these items are procurable in Vietnam are indicated below. Dust-proof garments are priority A, but being consumables, they were included in locally procured items

Items Eliminated from the Requested List	Priority
Dust-proof garments for clean area	A
Materials for clean room, Stainless worktables, maintenance tools	B
Glassware, Plastic materials, Metallic materials, Moving rack	C
PC bottle, Electric cleaner, Electric cleaner with HEPA filter, Personal computer, Carriage, Carriage (3 shelves), Table and lamp stand for visual inspection, Reagents, Stainless container, Equipment for Animal Laboratory, Candling set	D

The items listed in the table below are judged not necessary for the Measles Vaccine Production Facilities and have been eliminated from the procurement list.

Items judged not necessary
Liquid chromatography, Stopper handling unit, Printing machine
Electro spray lionization, Freeze dryer for QC, Air finder, Particle counter (hand held type)
Automatic potentiometic titrator, Electric dispenser (200cc)
Mercury vaporizer unit
Plasma sterilizer

2) Equipment Procurement List

The equipment to be procured under the Project is listed in Table 2-11 and Table 2-12. Furthermore, the specifications for the Main equipment are shown in Table 2-13.

Table 2-11 List of Equipment to be Procured under Grant Aid Funds

Serial number	Name of equipment	Priority	Qua.
1	Water supply unit	A	1
2	Rubber stopper washer	A	1
3	Vial washing machine	A	1
4	Dry sterilizing, cooling tunnel	A	1
5	Filling machine	A	1
6	Capping machine	A	1
7	Tray loading machine	A	1
8	Freeze dryer	A	1
9	Labeling machine	A	1
10-1	Laminar flow unit A	added	1
10-2	Laminar flow unit B	added	1
11	CO2 Incubator	B	2
12	Rotator for microtiter plate	D	2
13	pH meter	D	2
14	Safety cabinet	B	2
15	Dry oven	B	3
16-1	Incubator A	D	3
16-2	Incubator B	D	1
16-3	Incubator C	D	3
16-4	Incubator D	D	1
17-1	Centrifuge A	B	1
17-2	Centrifuge B	B	1
17-3	Centrifuge C	B	1
18	Endotoxin analyzer	B	1
19-1	Autoclave A	A	3
19-2	Autoclave B	A	2
19-3	Autoclave C for lab	B	6
20	Thermo-hygrometer	C	4
21-1	Moisture content apparatus	B	1
21-2	Drying oven for moisture titrator	B	1
22	Vacuum drying oven	added	1
23	Integrity test machine	B	3
24-1	Dryer A	D	1
24-2	Dryer B	D	1

Serial number	Name of equipment	Priority	Qua.
25	ELISA reader	B	1
26-1	Refrigerator(4℃)	D	3
26-2	Freezer(-30℃)	B	8
26-3	Deep freezer A(-70℃)	A	7
26-4	Deep freezer B(-70℃)	A	3
27-1	Bio guard clean bench A	A	2
27-2	Bio guard clean bench B	A	2
27-3	Bio guard clean bench C	A	1
27-4	Bio guard clean bench D	A	2
27-5	Bio guard clean bench E	A	4
27-6	Bio guard clean bench F	A	2
28	Cell counter(manual)	D	6
29-1	Microscope	D	3
29-2	Fluorescent-typed microscope	B	1
29-3	Inverted microscope	B	4
30-1	Water bath A	D	2
30-2	Water bath B	D	1
30-3	Water bath C	D	1
31	Hand washer	D	11
32-1	Electric dispenser A (10mL)	C	1
32-2	Electric dispenser B (100mL)	C	5
33-1	Compressor	D	7
33-2	Pump tubing	D	1
33-3	Vacuum pump	D	1
34	Osmometer	B	1
35	Stirrer、stand	D	1
36	Icemaker	D	3
37	N2 liquid stocker	D	1
38	Test tube mixer	D	7
39	Ultrasonic washer	added	1
40	Descicator	D	3
41-1	Electric balance A	D	1
41-2	Electric balance B	D	3
41-3	Electric balance C	D	1
41-4	Electric balance D	D	1
41-5	Electric balance E	D	1
41-6	Electric balance F	D	1
42	Table for electric balance	D	4
43	Weight for calibration	C	1
44	Draft chamber	A	1
45	Pipet washer	D	3
46-1	Pooling tank A (10L)	C	50
46-2	Pooling tank B (70L)	A	3
46-3	Pooling tank C (70L)	A	2
46-4	Pooling tank D (100L)	A	2
46-5	Pooling tank E (200L)	A	2
47-1	Egg incubator A	D	1
47-2	Egg incubator B	D	1
48	Incubator for egg stock	D	1
49	Plate washer	D	1

Serial number	Name of equipment	Priority	Qua.
50	Hot plate	D	1
51-1	Formalin perfusion system (dispersion)	B	4
51-2	Formalin perfusion system (decomposition)	B	2
52-1	Magnetic stirrer A	D	2
52-2	Magnetic stirrer B	D	1
53	Hand alcohol splay	D	20
54-1	Particle counter(for Air)	B	3
54-2	Particle counter(for water of injection)	B	1
55	Manual mixing device	D	1
56	Laundry machine	D	1
57	Drying machine	D	1
58	Total organic carbon analyzer	B	1
59	Conductivity meter	D	2
60	Air velocity meter	D	2
61-1	Constant temperature device immersion A	added	1
61-2	Constant temperature device immersion B	added	1
62	Disinfection tank	added	1
63-1	Sealer A	added	1
63-2	Sealer B	added	1
64	Portable pump	added	1
65	All the sinks	added	1
66-1	Filtration device for bacteria	A	3
	Filtration device for micoplasma	A	1
66-2	Pressure tank	added	3
66-3	Air sampler A	added	3
	Air sampler B	added	1
67	Recorder	added	7

Table 2-12 Equipment to be Procured by Vietnamese Funding

No.	Equipment	Priority
1	PC bottle	D
2	Electric cleaner	D
3	Electric cleaner (w/ HEPA filter)	D
4	Personal computer	D
5	Carriage (flat),Carriage w/ lift	D
6	Carriage (3 shelves)	D
7	Table & lamp stand for visual inspection	D
8	Pipettes	D
9	Stainless container (for sterilization)	D
10	Glassware: beakers, flasks, funnel, test tubes, glass tubing, cylinders, glass bottles, culture flasks, others	C
11	Plastic materials: polyethylene containers, centrifugal piping, rubber caps, thermal containers, others	C
12	Metallic materials: large bottles, stands, housing for filtration, others	C
13	Reagents, chemicals	D
14	Materials for clean room: Adhesive mats, liquid soap for automated hand washer, others	B
15	Dust proof garments	A
16	Machinery maintenance tools	B
17	Air-conditioner maintenance tools	B
18	Electronic Service Tools	B
19	Candling set	D
20	Shoe shelf	
21	Chair for clean room	
22	Locker A	
23	Locker B	
24	Stainless rack	
25	Moving shelf	
26	Moving rack	
27	Equipment for Animal Laboratory	
28	All the working tables	
29	Filtration filters	
30	others	

Table 2-13 Specifications of Main Equipment

No.	Description	Application	Specification, Dimension, etc.
1	Water supply unit	Unit that manufactures highly processed water (UF/WFI), water for injection and pure steam (PS).	Removing turbidity and particles, neutralizing, filtrating with active carbon and disinfecting with hydrogen chloride.
2	Rubber stopper washer	Washing rubber stoppers for vials with processed water	Washing ; rolling drum with UF/WFI
3	Vial washing machine	Roughly washing with UF and rinsing vials with WFI. Shifting them after draining with air blasting.	Dimension of vial ; 20≦X≦25mm , Operational rate ; 100～120(vials/min)
4	Dry sterilizing , cooling tunnel	Cooling after sterilizing vials form washing machine. Shifting them to filling machine.	Dimension of vial ; 20≦X≦25mm , Operational rate ; 100～120(vials/min) , Washing water of vials ; UF/WFI
5	Filling machine	Filling vaccine and water for injection separately. Stopping tightly for vaccine and stopping with half stopping for water for injection.	Dimension of vial ; 20≦X≦25mm , Operational rate ; 100～120(vials/min) , Plug ; stopper tightly/stopper with half stopping Filling ; vaccine and water for injection , Filling volume of vaccine ; 1.7ml ± 1% , Filling volume of water for injection ; 6.0ml ± 1%
6	Capping machine	Sealing by winding up vials that are already stopped tightly with thin aluminum metal.	Dimension of vial ; 20≦X≦25mm , Operational rate ; 100～120(vials/min) , Dimension of stopper ; less than 70mm , Supply of rubber stopper ; feed into the hopper by hand
7	Tray loading machine	Collecting vials filled with vaccine with half stopping of stopper into the tray. Feeding vials after freezing dry into the tray.	Dimension of vial ; 20≦X≦25mm , Operational rate ; 100～120(vials/min) , Collection of vials ; catch stitching , Inputting and outputting vials ; by hand
8	Freeze dryer	Freezing and drying vials filled with vaccine with half stopping of stopper.	Dimension of vial ; less than 25mm , Operational rate ; more than 30,000vials/batch , Minimum temperature on the shelf ; lower than -55℃ , Minimum temperature of condenser ; lower than -60℃ , Degree of vacuum ; 5～10×10^{-3}Torr , Placing vials ; put vials themselves on shelves , Integrity test ; off-line
9	Labeling machine	Applying labels to vials.	Dimension of vial ; 20≦X≦25mm , Operational rate ; 100～120(vials/min) , Length of label ; L15～220mm , H10～100mm , Detection of impress ; nil
10	Laminar flow unit A	Keeping cleanness by providing air through specified filters into limited area in the clean room owing to strictly controlling bacteria.	Class ; 100 , filter ; HEPA , Velocity ; more than 0.45m/sec , Flow ; up to down
11	Laminar flow unit B		
12	CO_2 Incubator	Culturing with the different CO_2 concentration in the clean room for virus culture.	Volume of chamber ; 165L*2=330L , Operating temperature ; 5～50℃ , CO_2 concentration ; 0～20%
13	Safety cabinet	Handling bacteria in the cabinet to keep them from being out of the cabinet.	Cabinet ; negative pressure , Evacuation ; outside of the building , Filter ; HEPA , Volume of evacuation ; more than 10m^3/min , Front of the cabinet ; safety glass
14	Dry oven	Sterilizing stainless instruments, glass instruments and siphon instruments with dry heat. Shifting instruments to the cleaner room.	Doors ; pass-through , Operating temperature ; max.300℃ , Volume of chamber ; 180L

No.	Description	Application	Specification, Dimension, etc.
15	Centrifuge A	Putting embryos out of chick's egg and trypsinizing them. Dividing them into cell by centrifuge.	Speed of rotation ; 300～5000rpm , Capacity ; more than 3000mL
16	Autoclave A (large size)	Sterilizing water for injection, stainless instruments and glass instruments with high steam pressure. It is used very often.	Doors ; pass-through , Sterilizing temperature ; 105～132℃ , Volume of chamber ; 4000L
17	Autoclave B (medium size)		
18	Integrity test machine	Supervising reliability of the filter by measuring a gas before and after filtration.	Floe rate ; 0.01～200ml/min , Test pressure ; 34～625kPa , Test gas ; compressed air , Operating temperature ; 4～50℃
19	Freezer A (-70℃)	Keeping bulk material in the stainless tank at -70℃.	Operating temperature ; －50～86℃ , Volume of chamber ; more than 480L
20	Freezer B (-70℃)		
21	Bio guard clean bench A	Keeping cleanness by providing air through specified filters into limited area in the clean room to allow to strict control of bacteria.	Class ; 100 , door ; one side , Filter ; HEPA , Capacity of collection ; more than 99.99% at the Particle of 0.3 μm , Air flow ; more than 15m^3/min , Initial flow rate from the filter ; more than 0.2m/sec , Width of cabinet ; W1300
22	Bio guard clean bench B		Class ; 100 , Door ; both sides , Filter ; HEPA , Capacity of collection ; more than 99.99% at the Particle of 0.3 μm , Air flow ; more than 18m^3/min , Initial flow rate from the filter ; more than 0.2m/sec , Width of cabinet ; W1300
23	Bio guard clean bench C		Class ; 100 , Door ; both sides , Filter ; HEPA , Capacity of collection ; more than 99.99% at the particle of 0.3 μm , Air flow ; more than 18m^3/min , Initial flow rate from the filter ; more than 0.3m/sec , Width of cabinet ; W1300 (attached with room for the dispensing tank , width ; 700)
24	Bio guard clean bench D		Class ; 100 , Door ; both sides , Filter ; HEPA , Capacity of collection ; more than 99.99% at the particle of 0.3 μm , Air flow ; more than 18m^3/min , Initial flow rate from the filter ; more than 0.3m/sec , Width of cabinet ; W1900
25	Bio guard clean bench E		Class ; 100 , Door ; both sides , Filter ; HEPA , Capacity of collection ; more than 99.99% at the Particle of 0.3 μm , Air flow ; more than 18m^3/min , Initial flow rate from the filter ; more than 0.3m/sec , Width of cabinet ; W2800
26	Bio guard clean bench F		Class ; 100 , Door ; both sides , Filter ; HEPA , Capacity of collection ; more than 99.99% at the particle of 0.3 μm , Air flow ; more than 18m^3/min , Initial flow rate from the filter ; more than 0.3m/sec , Width of cabinet ; W600

No.	Description	Application	Specification, Dimension, etc.
27	Fluorescent- typed microscope	Observing cell culture, tissue culture, growth of cell and so on.	Eyepiece ; 10× , Dimension of lens ; φ32 , Magnification ; 10-1500 , Stage stroke ; 40×70mm or more , Light source ; 12V Halogen lamp
28	Inverted microscope	Observing cell culture, tissue culture, growth of cell and so on.	Eyepiece ; 10× , 12.5× , 15× , Objective ; 4× , 10×, 20×, 40× , Stage stroke ; 50×70mm or more , Light source ; 12V Halogen lamp
29	Pooling tank for filling line（70L）	Mixing bulk material and diluting solution, providing them into the filling machine.	Inner surface of the chamber ; SUS316L , Stirring mechanism ; provided , Cooling mechanism ; provided , Viewport ; 2 , Intake made of hard glass ; 5 , Air vent ; 1
30	Formalin perfusion system (decomposition)	Decomposing the rest of the formic aldehyde gas with an oxidation catalyst after fumigating clean rooms and air conditioning facilities with formic aldehyde gas.	Process ; catalytic combustion system , Process capacity ; more than 300m^3/h Process volume ; more than 100m^3 Process time ; 5～6hours
31	Particle counter for water of injection	Measuring particles in the water for injection.	Measuring particle size ; 0.7～133μm Light source ; semiconductor laser Suction volume ; 5～100mL/min
32	Laundry machine	Laundering of garments for clean rooms. It is used very often and contains specific filters to maintain cleanness of the laundry chamber.	Process volume ; more than 8kg Water ; UF , Application ; used in the clean room , Inner surface ; SUS304
33	Drying machine	Laundering of garments for clean rooms. It is used very often and contains specific filters to maintain cleanness of the laundry chamber. Negative pressure keeps particles from dispersing.	Process volume ; more than 8kg Drying ; electric system , Filter ; HEPA , Inner chamber ; negative pressure , Application ; used in the clean room
34	Total organic carbon analyzer	Analyzing minute amount of organic carbon in the water of sample highly precisely. Supervising reliabilities of water for injection itself and filters.	Carrier gas ; highly purified air , Measuring range ; TOC4ppb～10,000ppm , Sample volume ; 4～400μL , Measuring principle ; oxidation/NDIR detector

(8) Vaccine Production Process Planning

1) Production Plan

Based on analysis in Japan, the annual production of measles vaccine has been set at 7,500,000 doses annually. An operation schedule for annual production of 7.5million doses was set out and a simulation for annual production was conducted. The simulation was based on the following assumptions.

<Assumed Operating Conditions>

- Annual operation days: 260 days/year
- Freeze dryer capacity: 30,000 vials/lot
- Filling time: 1 day
- Freeze drying time: 6 days
- SIP/CIP* time: 2 days
- Bulk amount used for 1lot filling and freeze drying: 20 L

・Produced amount for 1lot bulk process: 40～60 L

・Loss of bulk manufacturing process: 25 %

・Loss of filling and freeze drying process: 10 %

*SIP/CIP: Sterilization in place / Cleaning in place

The calculated annual production volume for single freeze-dryer and 2 freeze-dryer lines are shown below:

a) Case with one freeze-dryer line: 756,000 vials annually (7,560,000 doses)

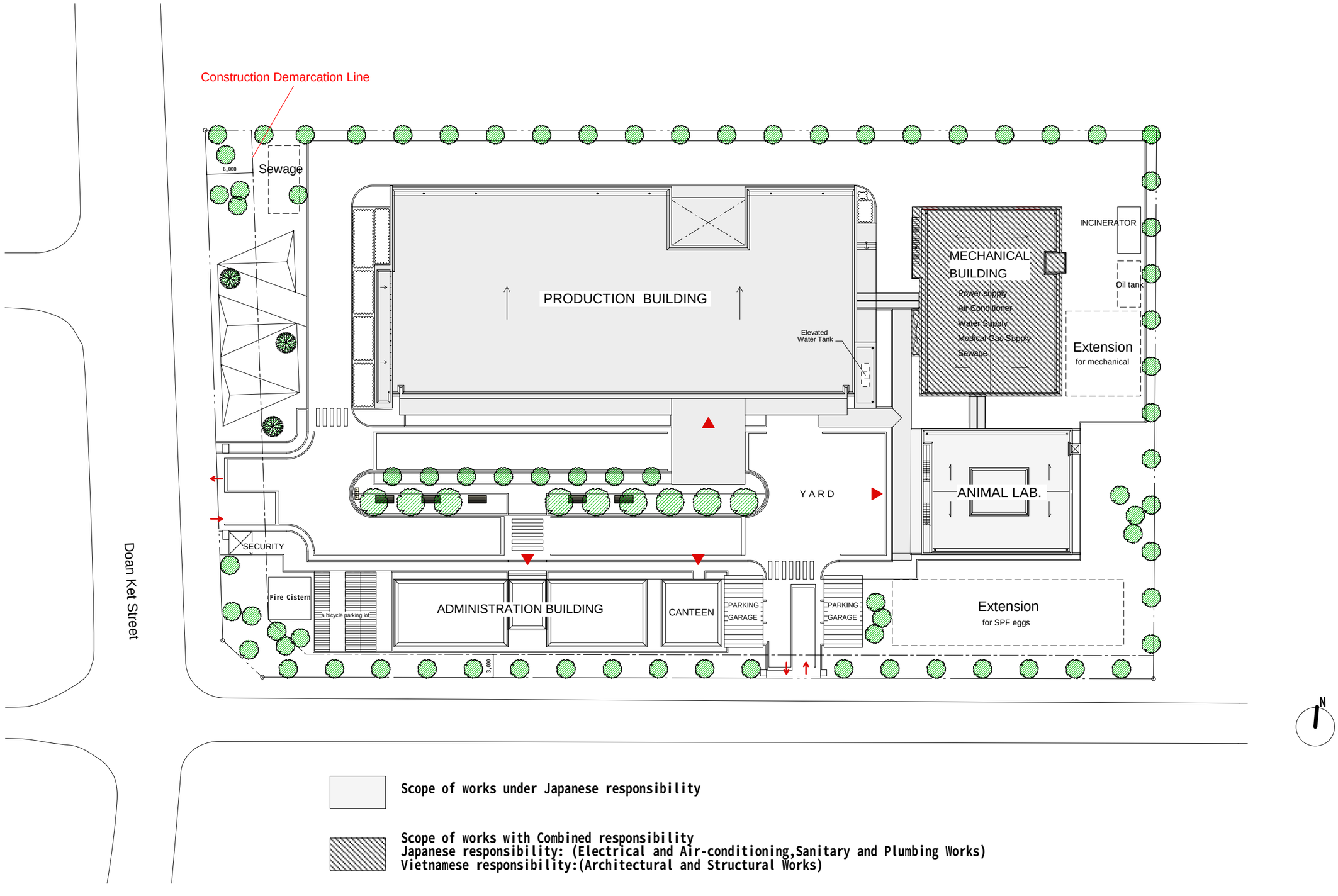
b) Case with two freeze-dryer lines: 1,215,000 vials annually (12,150,000 doses)

2-2-3 Basic Design Drawings

Basic Design Drawings are enclosed in the following pages.

Table 2-14 List of Drawings

	Building	Title of Drawing	Scale	Page
①	Facility Layout	Site Plan	1/500	53
②	Production Building	First Floor Plan	1/200	55
③		Second Floor Plan	1/200	57
④		North and South Elevations	1/200	59
⑤		East and West Elevation	1/200	61
⑥		Sections	1/200	63
⑦	Animal Laboratory	Plan, Elevations and Sections	1/200	65
⑧	Mechanical Building	Plans	1/200	67
⑨		Elevations and Sections	1/200	69

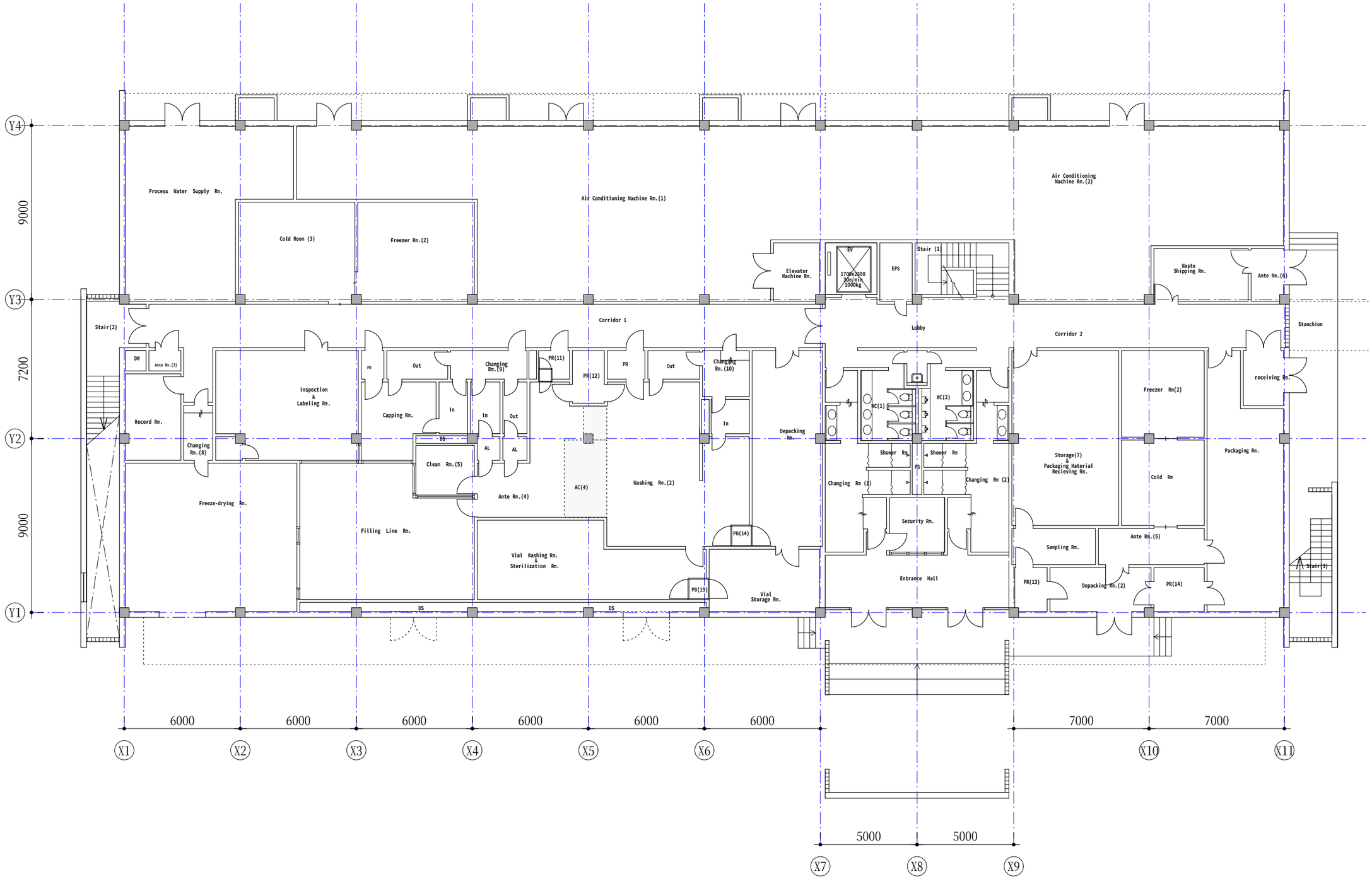


Scope of works under Japanese responsibility

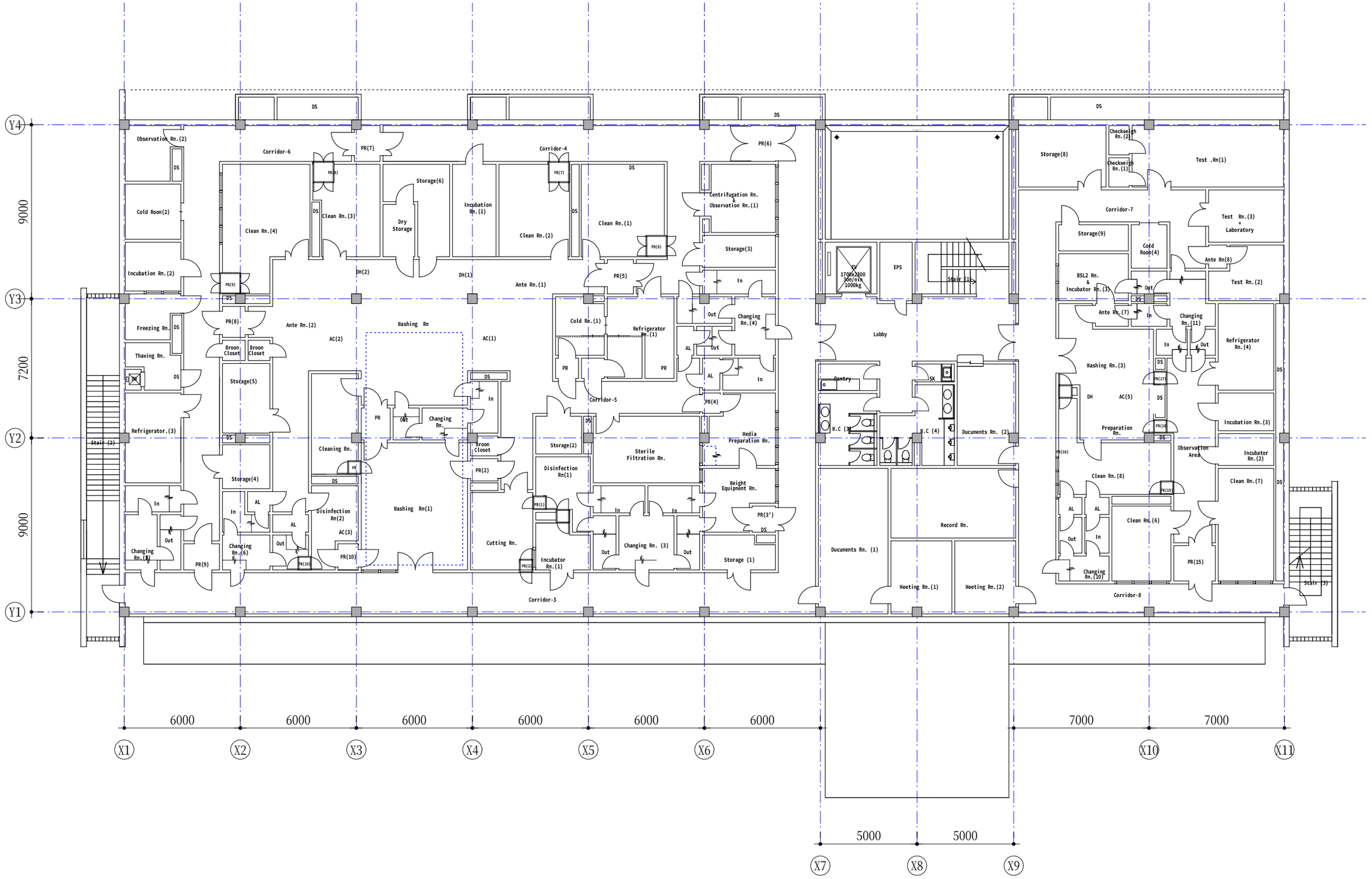
Scope of works with Combined responsibility
Japanese responsibility: (Electrical and Air-conditioning,Sanitary and Plumbing Works)
Vietnamese responsibility:(Architectural and Structural Works)

Scope of works under Vietnamese responsibility

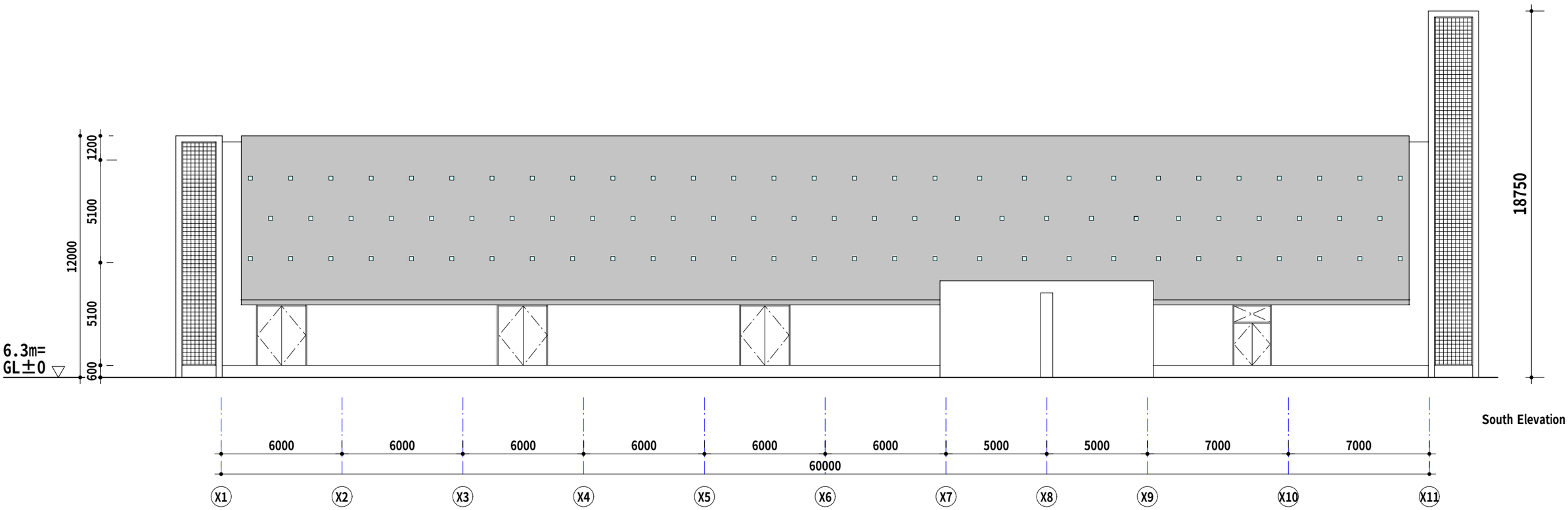
Facility Layout		
Title	Scale	Page No.
Site Plan	1/500	53



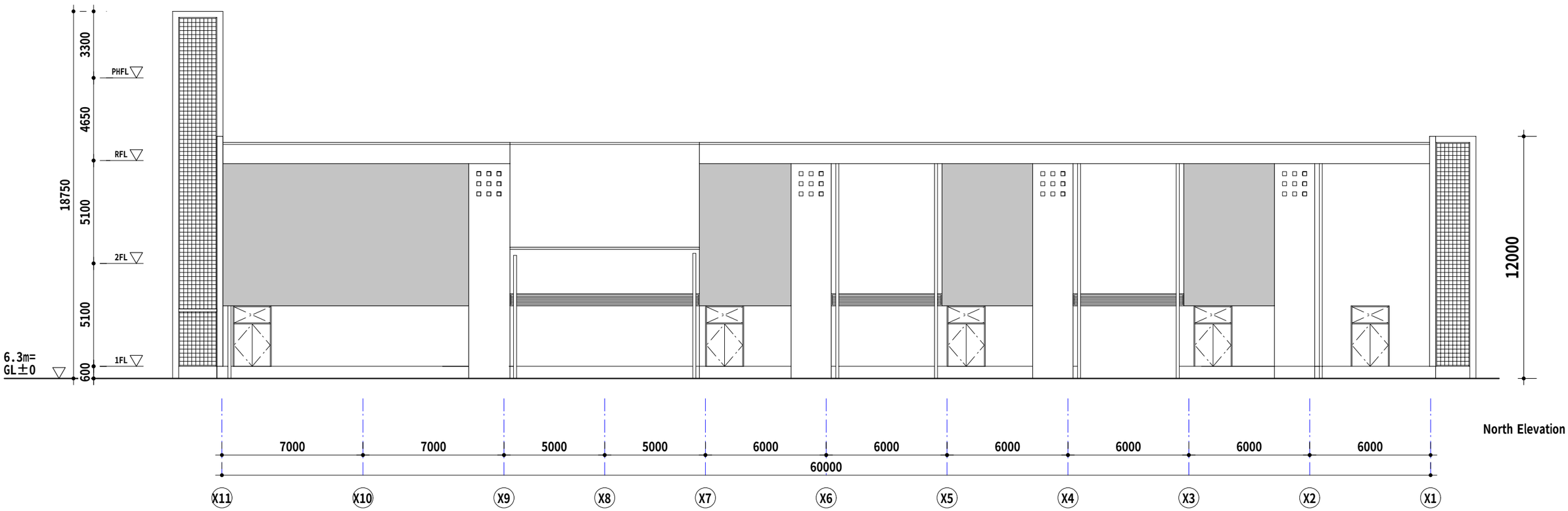
Production Building		
Title	Scale	Page No.
First Floor Plan	1/200	55



Production Building		
Title	Scale	Page No.
Second Floor Plan	1/200	57

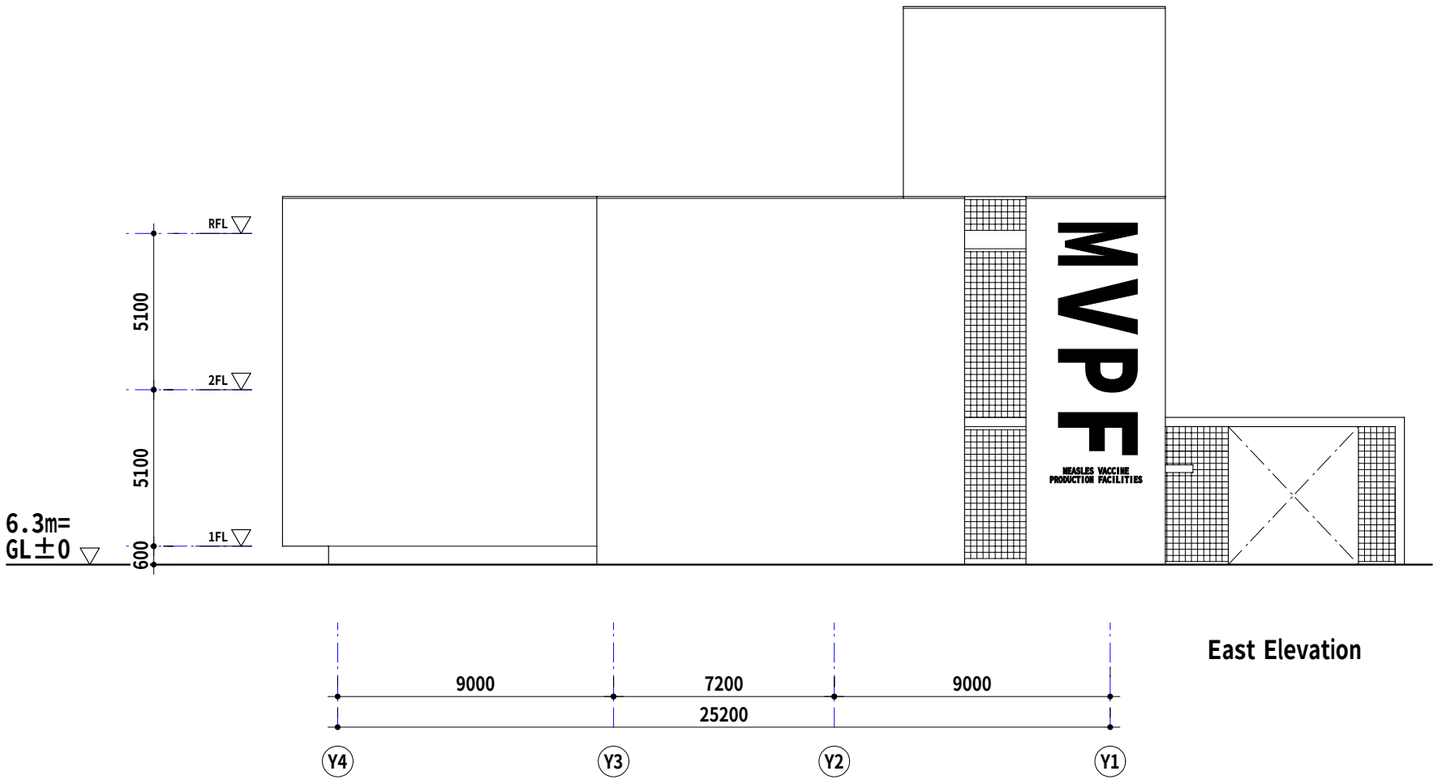


South Elevation

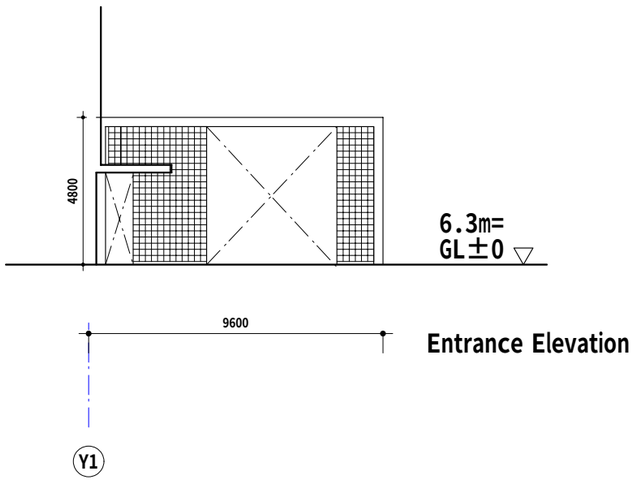


North Elevation

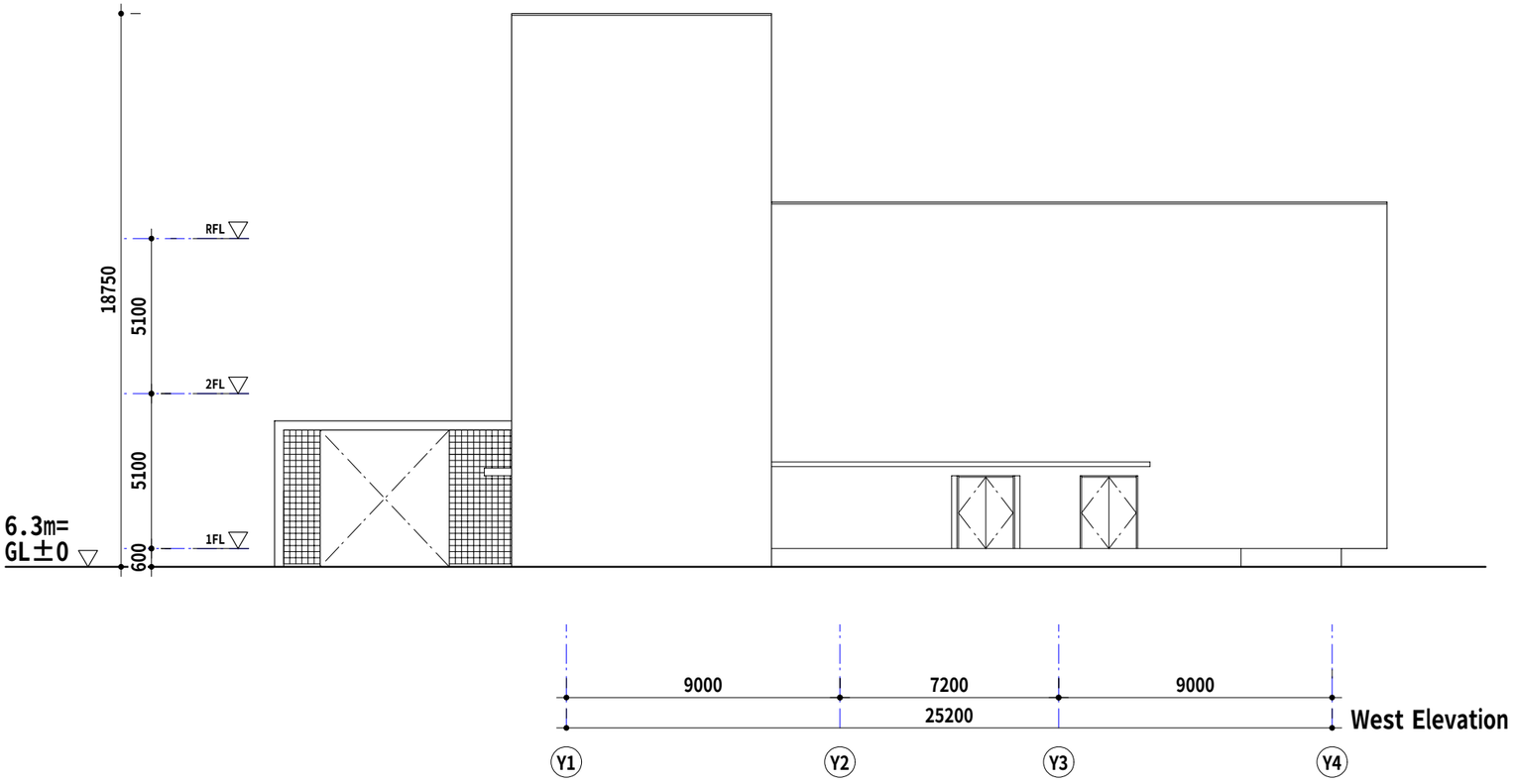
Production Building		
Title: North and South Elevations	Scale: 1/200	Page No.: 59



East Elevation

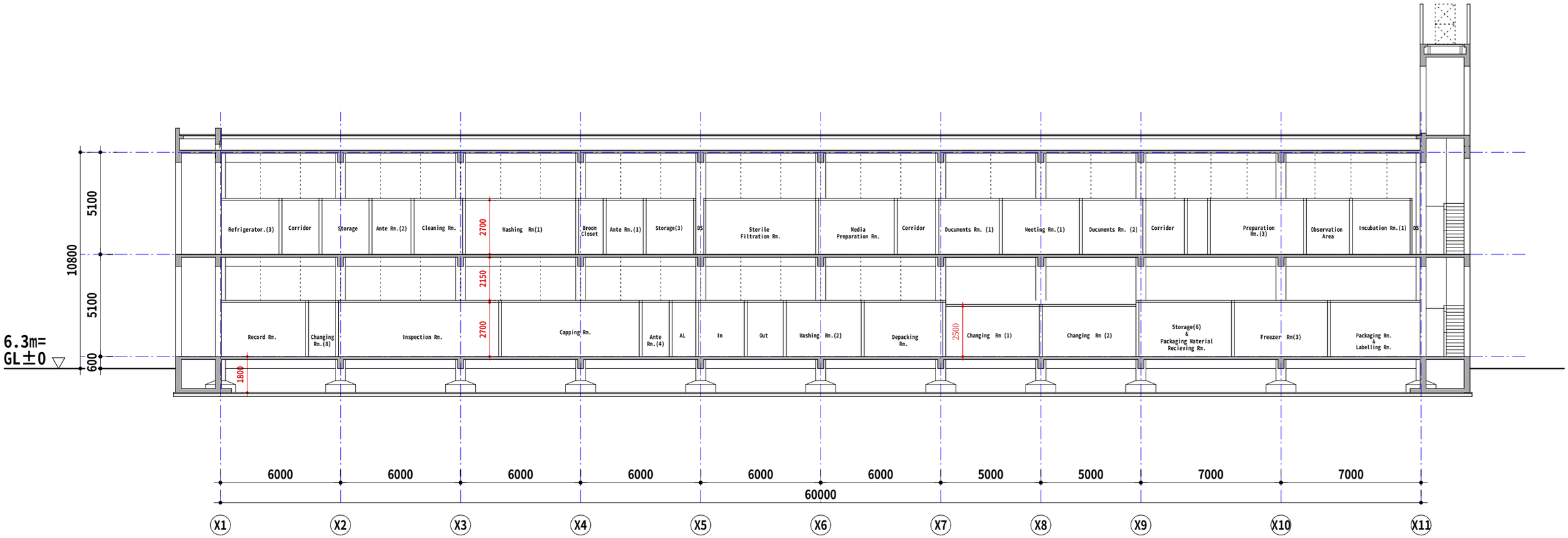


Entrance Elevation

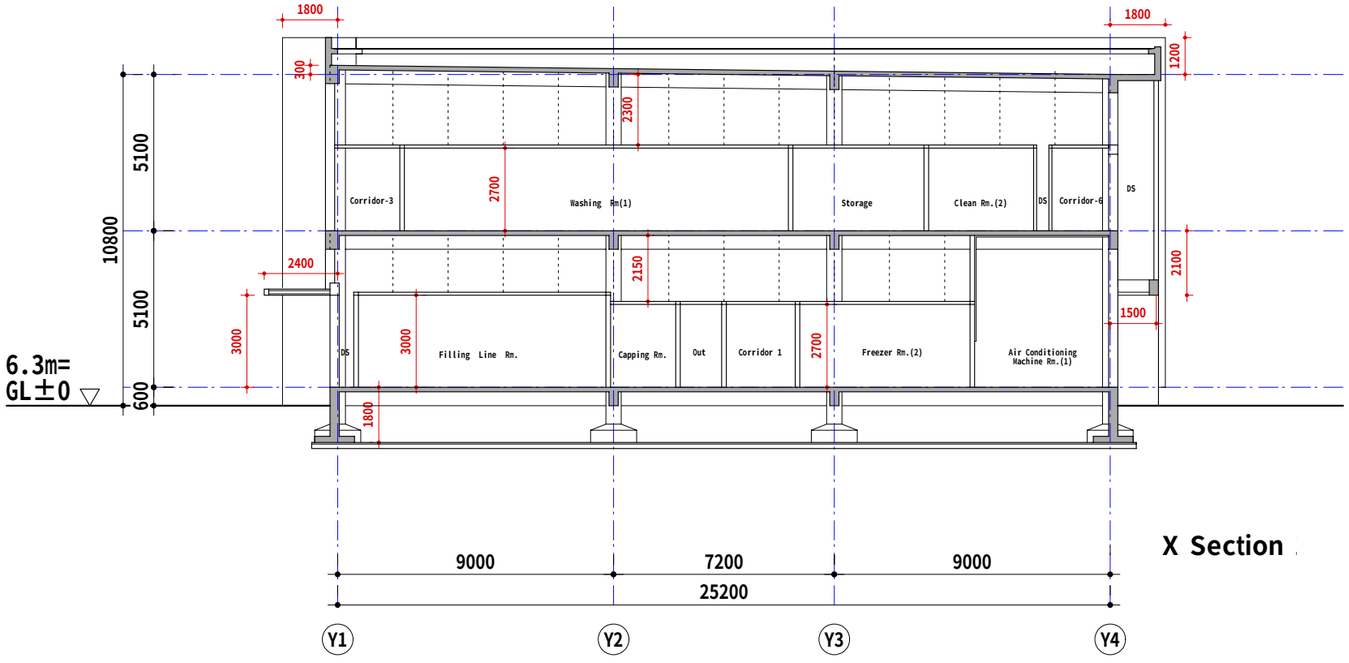


West Elevation

Production Building		
Title East and West Elevations	Scale 1/200	Page No. 61

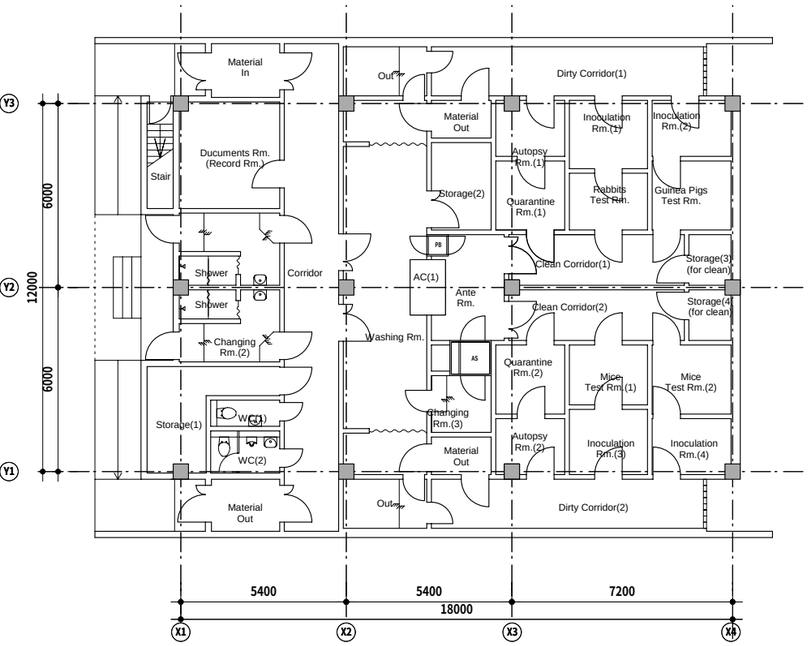


Y Section

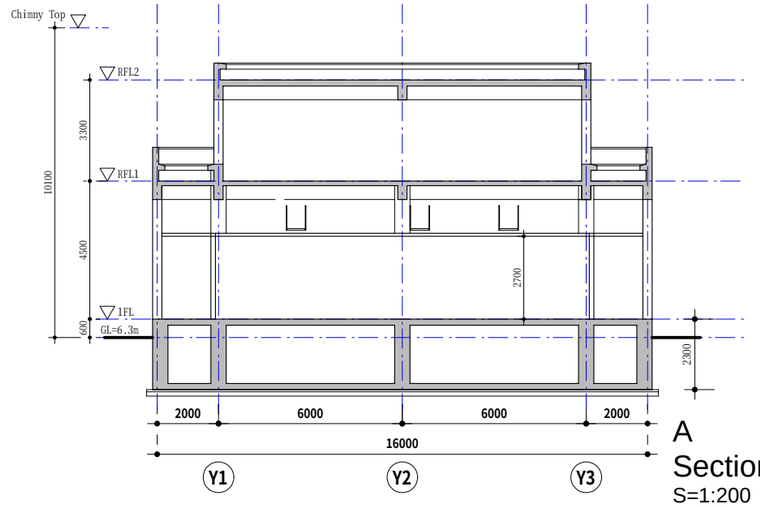


X Section

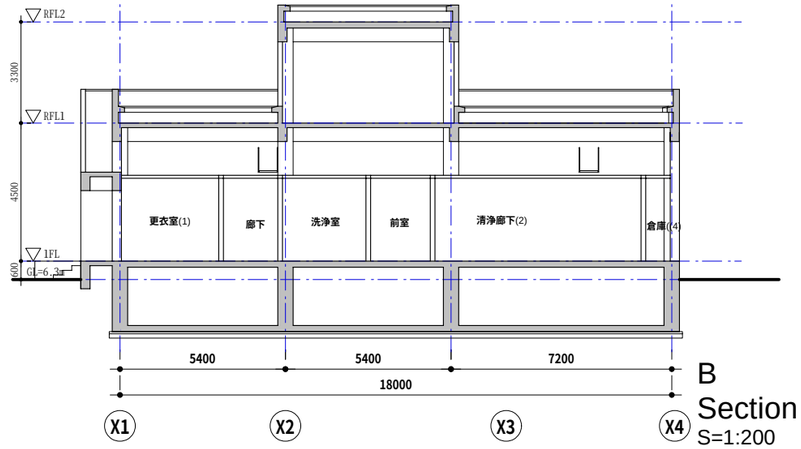
Production Building		
Title: Sections	Scale: 1/200	Page No.: 63



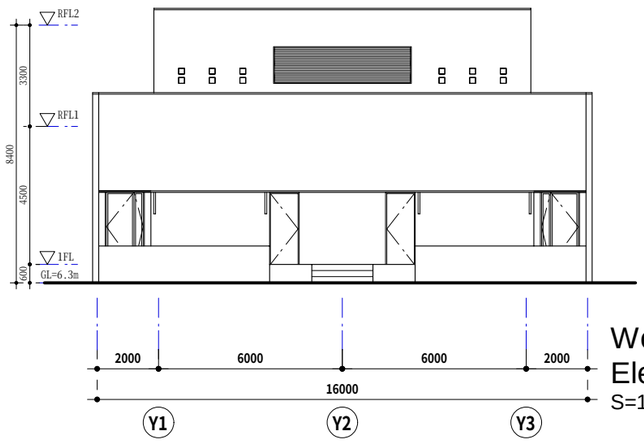
Plan
S=1:200



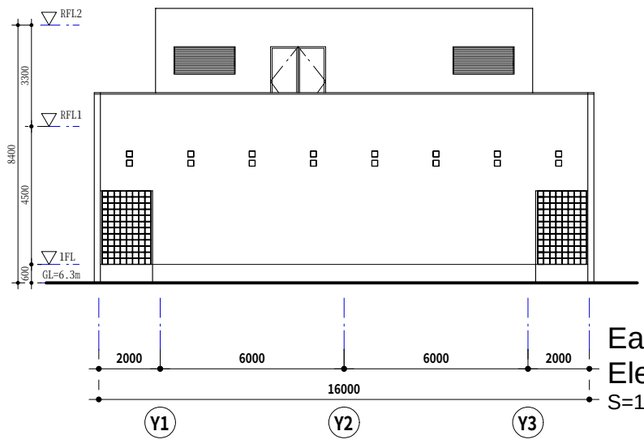
A
Section
S=1:200



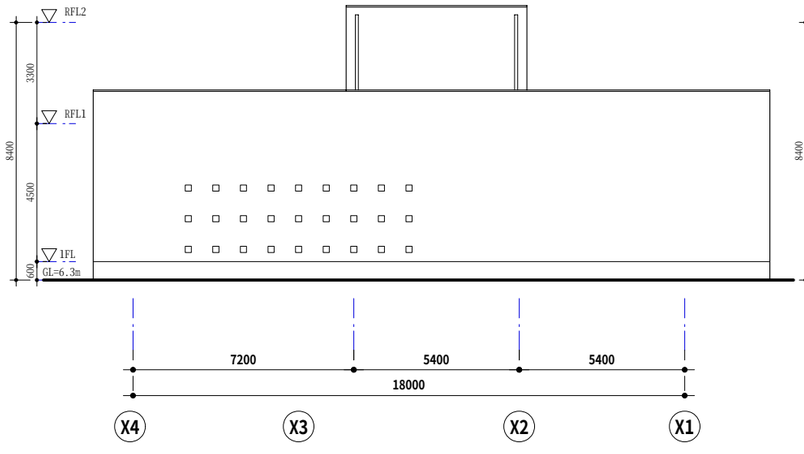
B
Section
S=1:200



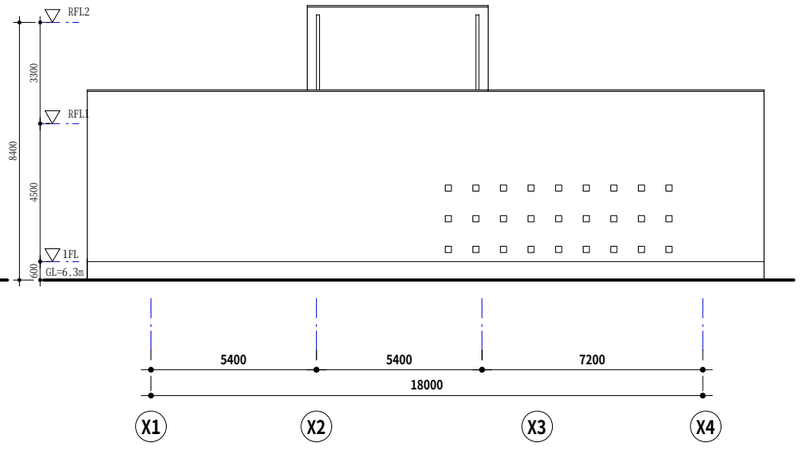
West
Elevation
S=1:200



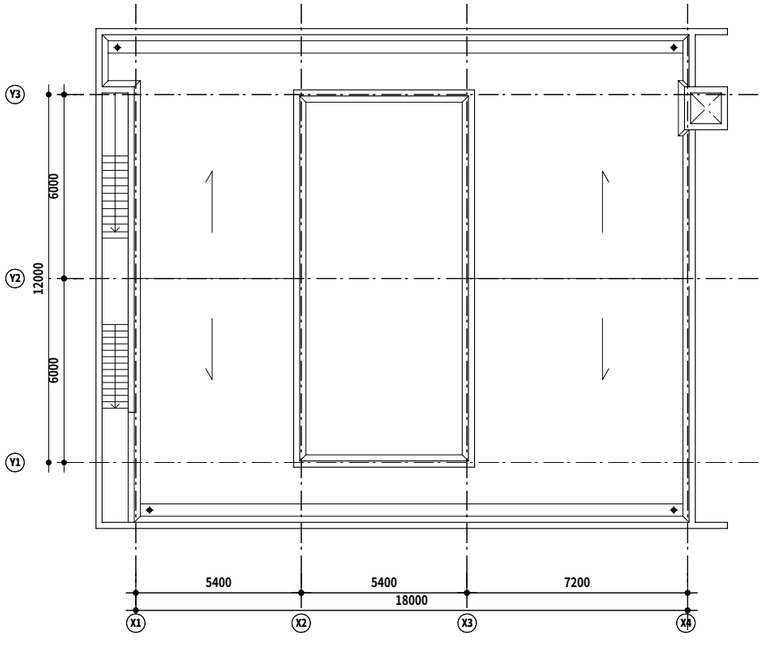
East
Elevation
S=1:200



North Elevation S=1:200



South Elevation S=1:200



Roof Plan S=1:200

Animal Laboratry		
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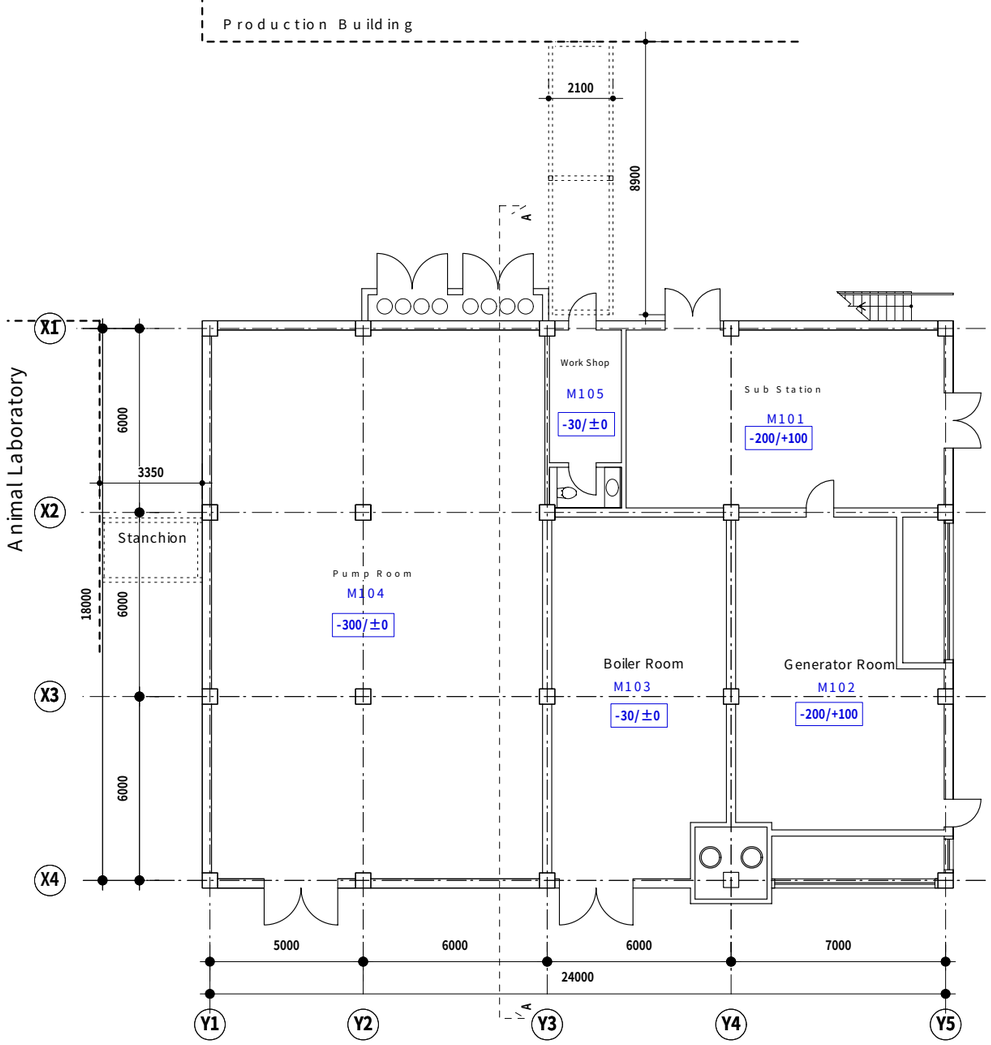
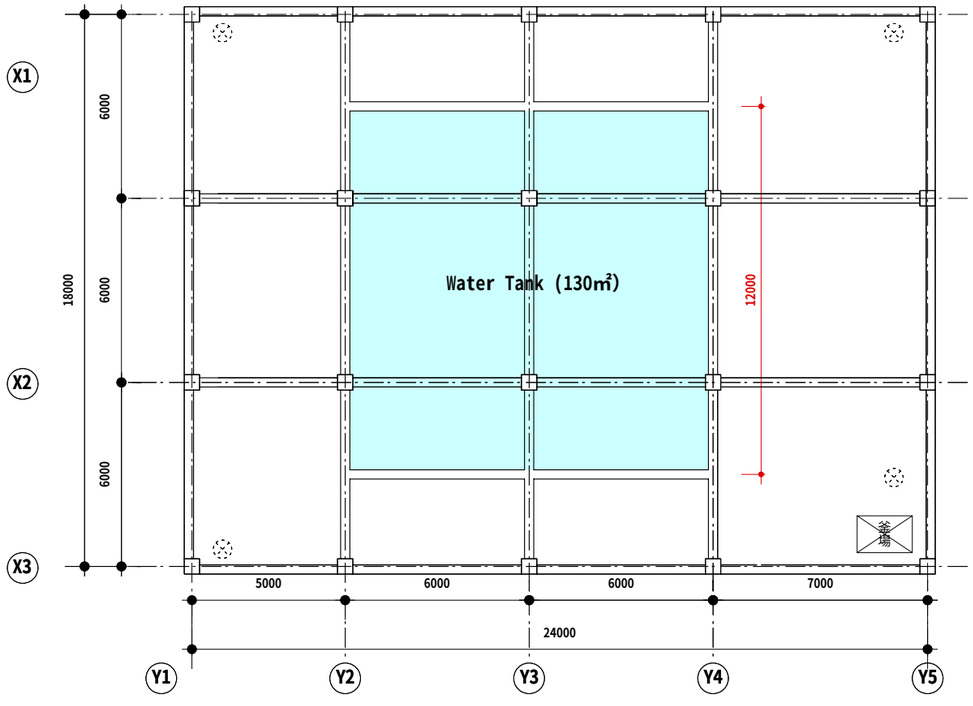
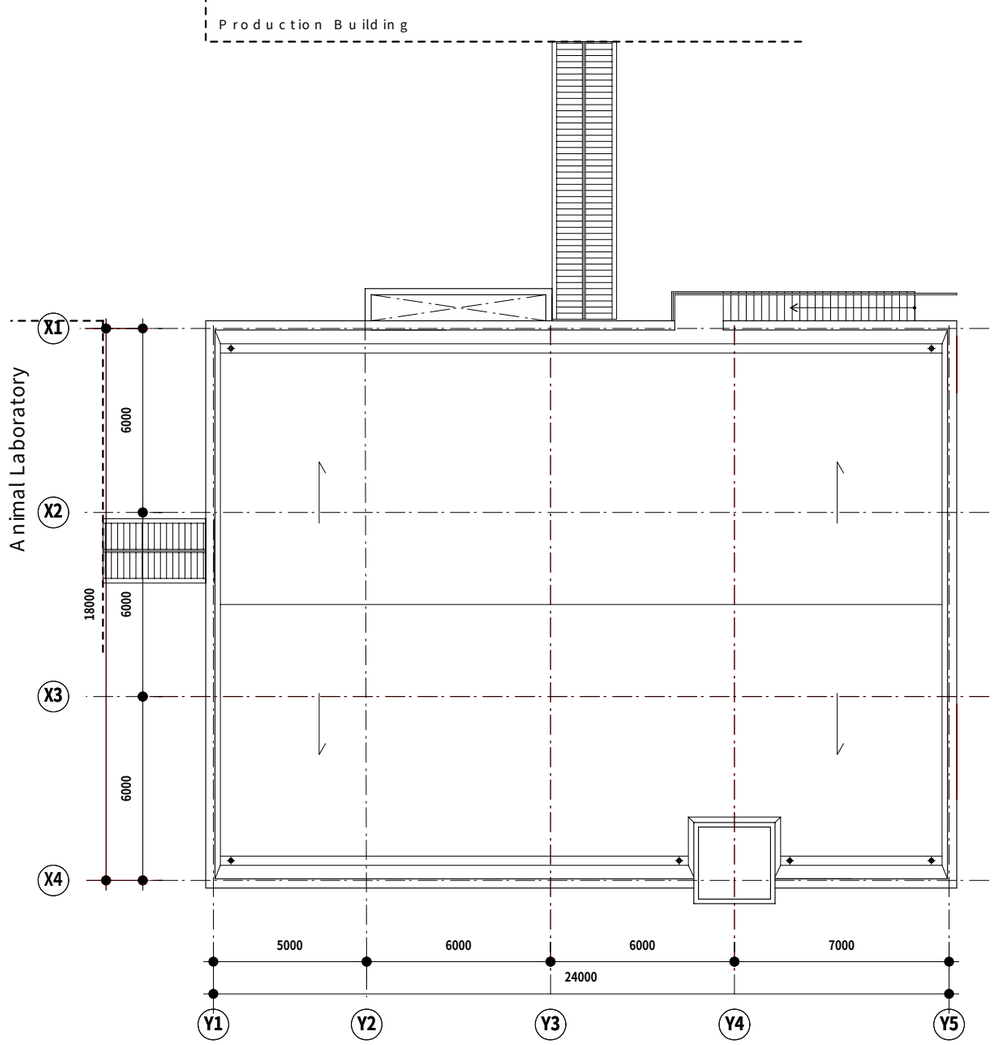


1st Floor Plan



Pit Floor Plan



Roof Plan

Mechanical Building		
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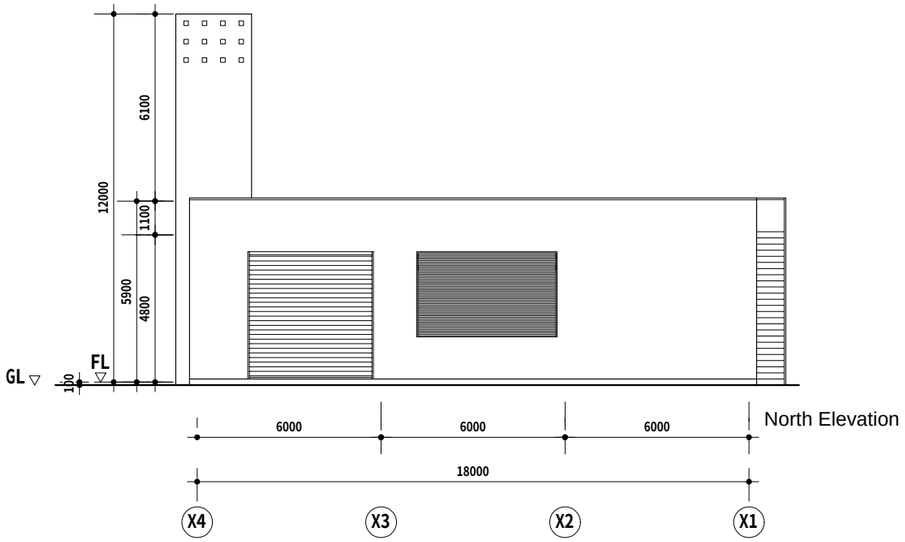
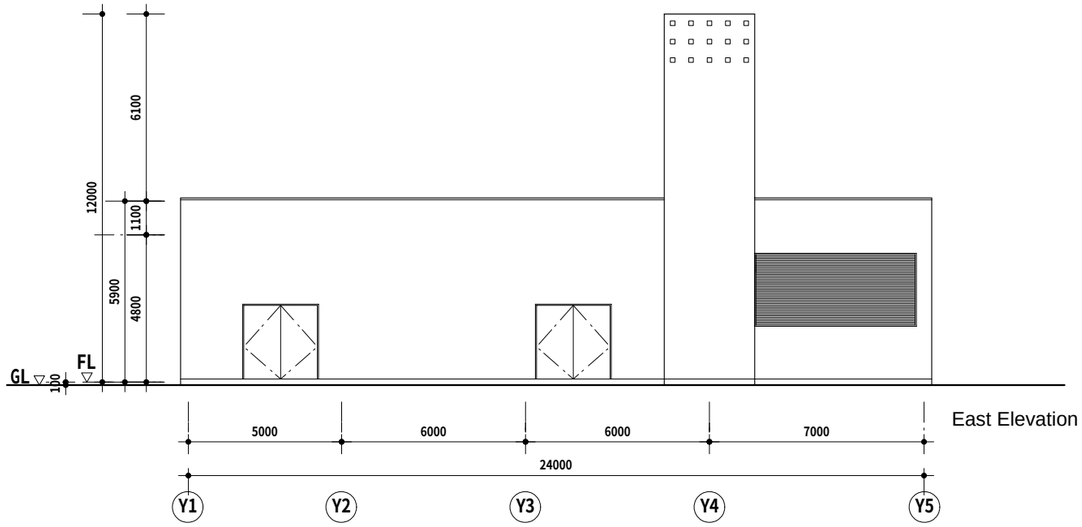
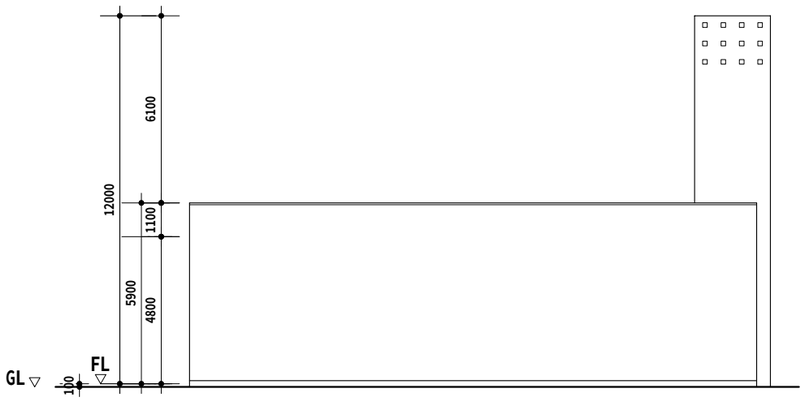


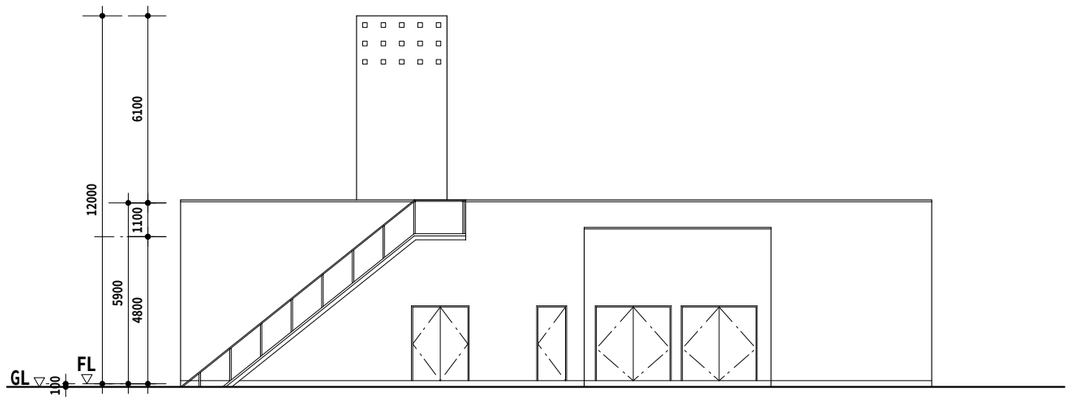
North Elevation



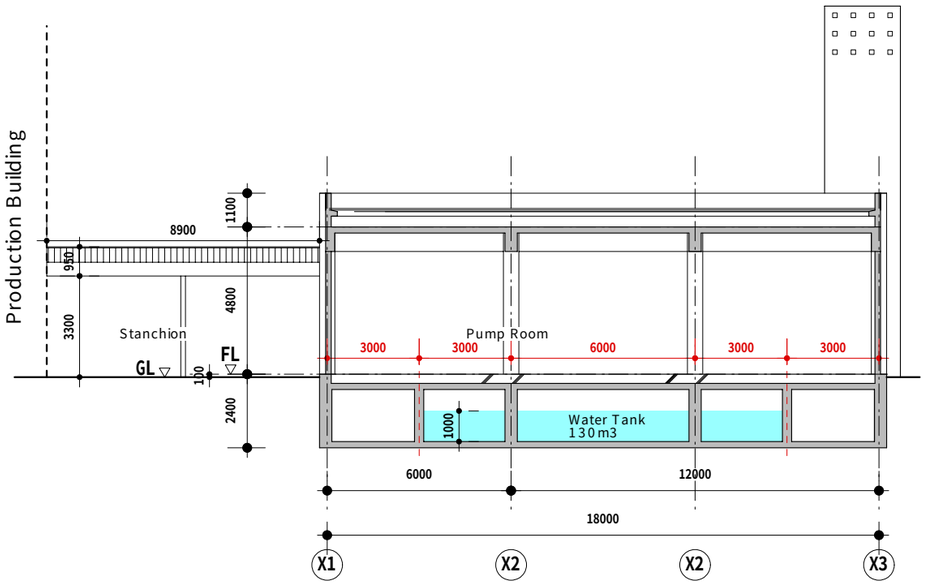
East Elevation



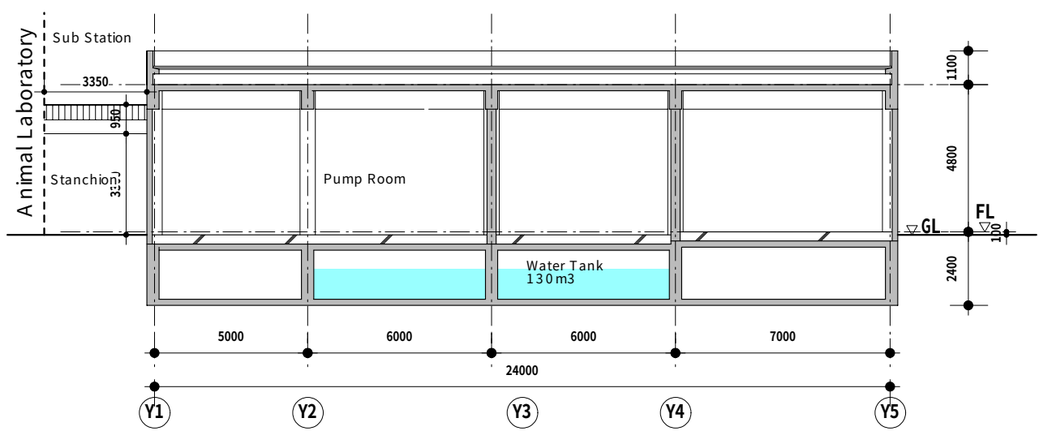
South Elevation



West Elevation



A Section



B Section

Mechanical Building		
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