B-03

April 1, 2004

Guidelines on the Preparation of Documents for Obtaining Certification of GLP Compliance (advance)

- These are the guidelines on how to prepare the documents to be attached to an application for GLP certification for testing facilities or to be submitted prior to the inspection. Since we need to read these documents beforehand, please prepare and submit the prescribed number of copies of them by the prescribed due date.
- These documents will be used for a preliminary hearing, explanation for the outline of the facility on the first day of the inspection, on-site inspection tour, and hearing with the testing facility manager etc.
- Print the documents vertically on A4-size paper and bind them on the left side. A4-size paper should be used for all the documents, including the layout plans of the facility. (However, if we find any document difficult to read in A4 size after they have been submitted, we might ask you to print it horizontally on A3-size paper and to fold it into A4 size.)
- In principle, the documents should describe the situation as of the time when the documents are prepared. (However, if the state of the facility inspected as of the date of inspection is going to be greatly different from the situation as of the time when the documents were prepared, we might ask you to prepare a comparative table listing the differences.)
- Photographs to be attached to the documents may be substituted with photo-quality copies thereof.
- A table of contents should be attached to the documents, all the pages of which should be numbered sequentially. No segmentation such as indexing is necessary.

* In the case of a document for which a series of formats has been created, if you prepare the document in accordance with the formats, you do not need to prepare a table of contents.

- The documents should contain detailed but concise descriptions of the facility.
- If different sets of GLP regulations use different terms to mean the same thing, those terms may be stated side by side.

The following abbreviations are used herein.

Law on incorporated administrative agency - PMDA: Law on PMDA

Law on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc.: Law on Chemical Evaluation

Law on Industrial Safety and Health: Law on Industrial Safety

Law on Safety Assurance and Quality Improvement of Feed: Law on Feed Safety

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26. Environmental control of important zones and the monitoring procedures

27. Washing and disinfection procedures

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(2) Handling of diseased animals and animals presenting disease-like symptoms

(3) Management of feed, water, animal care instruments, detergents, etc.

29. Master schedule

30. Standard Operating Procedures (SOPs)

(1) Copy of SOPs and formats prescribed in SOPs

(2) Preparation, revision, abolishment, etc. of SOPs

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31. Flowchart of safety (toxicity) studies

32. Outline of computer system

33. Commissioning of studies to outside organizations

34. Recommendations made in the last GLP inspection and recent improvements

1. Testing facility subject to inspection

(1) Name (in Japanese and English)

If the testing facility inspected is spread across different locations, the name of the facilities in each location should be stated.

(Example)

XX *Kabushiki Kaisha*, XX *Kenkyujo*.

(English) XX Institute, XX Company Limited

(2) Location (in Japanese and English)

If the testing facility inspected is spread across different locations, the address of each location should be stated.

(Example)

XX-ken, XX-shi, XX, 1-2-3

(English) 1-2-3, XX, XX, XX

2. Inspection date

(Example) XX, XX, XX to XX, XX, XX (X days)

3. Purpose, etc. of inspection

(Example 1) To conduct an inspection to certify GLP compliance of the testing facility, based on the application submitted to the Director-General of XX (Chairperson).

(Example 2) To conduct an on-site inspection to certify GLP compliance of the documents attached to the application for approval of a drug for XX.

4. Fields or items of studies

* The “fields or items of studies” should be interpreted as “Fields of tests” in the case of an application filed under the Law on Agricultural Chemicals Control, as “Items of tests” under the Law on PMDA, the Law on Chemical Evaluation, or the Law on Industrial Safety, and as “Types of tests for which GLP certification is sought” under the Pharmaceutical Affairs Law (pharmaceuticals for animals).

* In the case of an application filed under the Law on Chemical Evaluation (enrichment studies or toxicity studies only), in order to request GLP certification for some enrichment studies or toxicity studies, the applicant shall specify each of the studies subject to the application (e.g. enrichment

study (1-octanol/water partition coefficient test) or toxicity study (twenty-eight day repeated dose toxicity study)).

* In the case of an application filed under the Pharmaceutical Affairs Law (pharmaceuticals for animals), if the applicant seeks GLP certification for a study that has been suspended for the last three years or longer or a study that has not been conducted although it is practicable, the applicant shall specify the fields or items of the study.

* In the case of an application filed under the Law on Agricultural Chemicals Control or the Law on PMDA, the fields or items of practicable studies should also be stated.

5. Studies subject to the application

(1) Make the table containing title, number, GLP applicated to study, test item (Code or synonym is acceptable), Study Director, study initiation date, study completion date and remarks (if any). The studies should be broken down by the test item or the type.

(Example)

Study field	Title and number of study	GLP applicated to study	Test item	Study Director	Study initiation date	Study completion date	Remarks
XXX study	XX study. A001	(Industrial chemical) (Pharmaceutical)					
	XX study. A002	(Work place)					
OOO study	OO study B001	(Agricultural)					

(2) State the number of studies conducted in the past ten years. The number should be broken down by the type and year of the study. The number should be also broken down by GLP and non-GLP studies.

* The year in which a study is commenced should be deemed as the year of the study.

(Example)

Number of studies (last ten years)

Type of study Year	XX study	XX study	
XXX	X (including 000 GLP	X (including 000 GLP	

	applicable studies X)	applicable studies X)	
XXX	X (including 000 GLP applicable studies X)	X (including 000 GLP applicable studies X)	
XXX	X (including 000 GLP applicable studies X)	X (including 000 GLP applicable studies X)	

6. Rules for conducting internal audit and status of internal audit in the past three years

State the rules regarding internal audit.

State the number of internal audit in the past three years. The number should be broken down by the study (status of conducting studies, final report, etc.), facilities and year, respectively.

(Example)

Internal audit is provided in SOPs as below.

SOP number	Title
SOP/QAU/XXX	Task of QAU
…	…

Status of internal audit in the past three years

Internal audit concerning studies (number)

Year	Audit items	OO study	XX study	YY study	ZZ study
	Study plan				
	Status of conducting study				
	Final report				
	…	…	…	…	…
	…	…	…	…	…

Internal audit concerning facilities (number)

Year	Equipment, instrument	Test item, reagent	Archive	Waste	Education/ training	Remarks ( )

7. Historical background (important events such as the establishment of the facilities, beginning of GLP applicable studies, authorities' inspections and inspection results)

Describe the history of the testing facility (establishment, relocation, merger with another department, etc.). Indicate the year when GLP applicable studies begun to be carried out.

A. The year and month in which the testing facility was established

B. The purposes of establishment

C. The entity that established the facility

D. The year and month in which GLP applicable studies begun to be carried out (for each type of study)

E. The name of the computer system, the year and month in which development of the system started, the year and month in which implementation (operation) of the system started

F. The year and month in which the authorities conducted a GLP inspection, inspection results, and the notification date of the results

G. Extension or reconstruction of facilities (if this is not the first GLP inspection, the applicant shall clearly describe any extension or reconstruction of the facilities that has been made since the last inspection)

(Example)

Month/Year	Events
	Established as a clinical testing company in XX city, XX prefecture The laboratory relocated to YY city, YY prefecture and was renamed as the Safety Research Center Obtained GLP conformance for XX study and YY study Extended the SPF animal facilities (rats and mice) Renamed as the Safety Research Institute and restructured into one division with three offices as the result of a structural reform Obtained GLP conformance for XX study Introduced a central system to manage study data and animal housing facilities Underwent a GLP inspection of YY conducted by ZZ Ministry (inspection results notified on XX, X, XXXX, evaluated as XX) Obtained GLP conformance for ZZ study Construction of archiving facilities Alteration of the central system to manage study data and animal housing facilities Underwent a GLP inspection of XX conducted by YY Ministry (inspection results notified on XX, X, XXXX, evaluated as XX) Reconstructed the SPF animal facilities (rats and mice) and extended rabbit housing facilities

8. Article of an association or act of endowment

Attach the copy of the article of an association or act of endowment.

9. Photograph or illustration of the entire premises of the facility and layout plan of the buildings (floor plan of the testing facility)

(1) Photograph or illustration of the entire premises of the facility

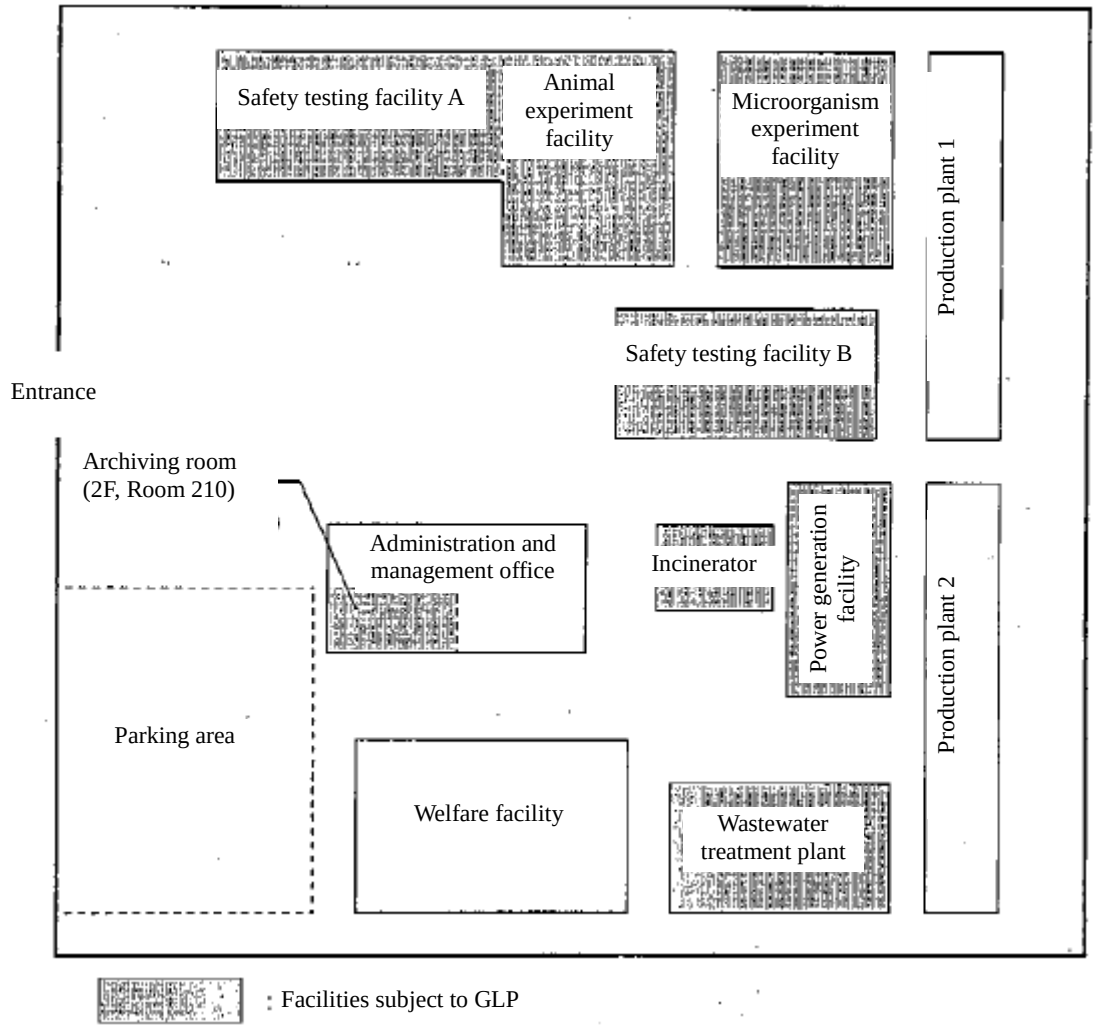
Provide a photograph or illustration that shows not only the facilities subject to inspection but also the overview of the entire premises (including factories and other facilities within the premises).

(Example) Attach a photograph or illustration.

(2) Layout plan of the buildings (floor plan of the testing facility)

Provide a layout plan of the buildings. It does not have to be an accurate drawing made to scale: a sketch detailed enough to show the layout of the facilities would suffice. Specify the name, room number, etc. of each type of facility subject to GLP regulations (if only part of the facilities is subject to GLP regulations, that specific part should be identified). Mark each type of facility with different shades, dots, bold lines or colors.

(Example)


Safety testing facility A
Animal experiment facility
Microorganism experiment facility
Production plant 1
Safety testing facility B
Entrance
Archiving room (2F, Room 210)
Administration and management office
Incinerator
Power generation facility
Production plant 2
Parking area
Welfare facility
Wastewater treatment plant
: Facilities subject to GLP

10. Area

Indicate the area of the testing facility.

(Example) Area of the site XXX m^2

11. Number of stories and total floor area of each building that houses facilities

Indicate the number of stories and the total floor area of each building that houses facilities and also indicate the total floor area of all the buildings.

Calculate the floor areas of the GLP zone and non-GLP zone, respectively.

State the applicable GLP in the remarks column, if facilities can operate two or more types of GLP study.

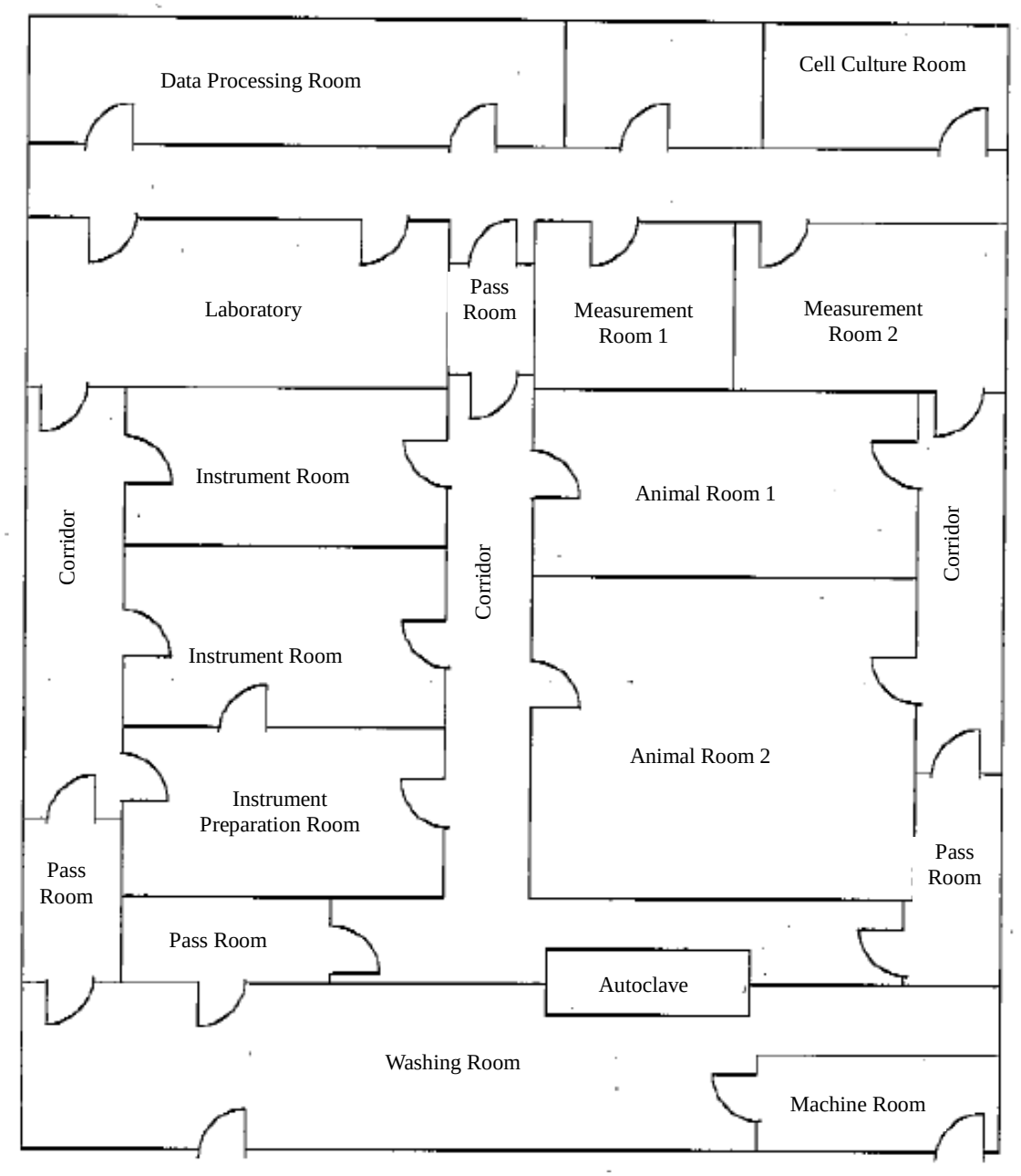
(Example)

Facility name	Number of stories	Floor area			Remarks
		GLP zone	Non-GLP zone	Total	
Research Building	X-story building	XX m^2	XX m^2		
XX Laboratory	Xth floor			XX m^2	
Archiving Room	Xth floor			XX m^2	
Staff Room	Xth floor			XX m^2	
Animal Building	X-story building	XX m^2	XX m^2		
Housing Room	Xth floor			XX m^2	
Anatomy Room	Xth floor			XX m^2	
Feed Mixing Room	Xth floor			XX m^2	
Pathology Room	Xth floor			XX m^2	
Microscopy Room	Xth floor			XX m^2	
Administration Building	X-story building	XX m^2	XX m^2		
Administration Office	Xth floor			XX m^2	
Quality Assurance Room	Xth floor			XX m^2	
Waste Storage	Xth floor			XX m^2	
Wastewater Treatment Plant	Xth floor			XX m^2	
Total Floor Area		XX m^2	XX m^2	XX m^2	

12. Floor layouts of each building (layout plans of major facilities, equipment, etc.)

Present floor layouts of each building indicating the locations of major facilities and equipment. Attach the photograph, as necessary.

(Example)



13. Organization and personnel of the testing facility, etc.

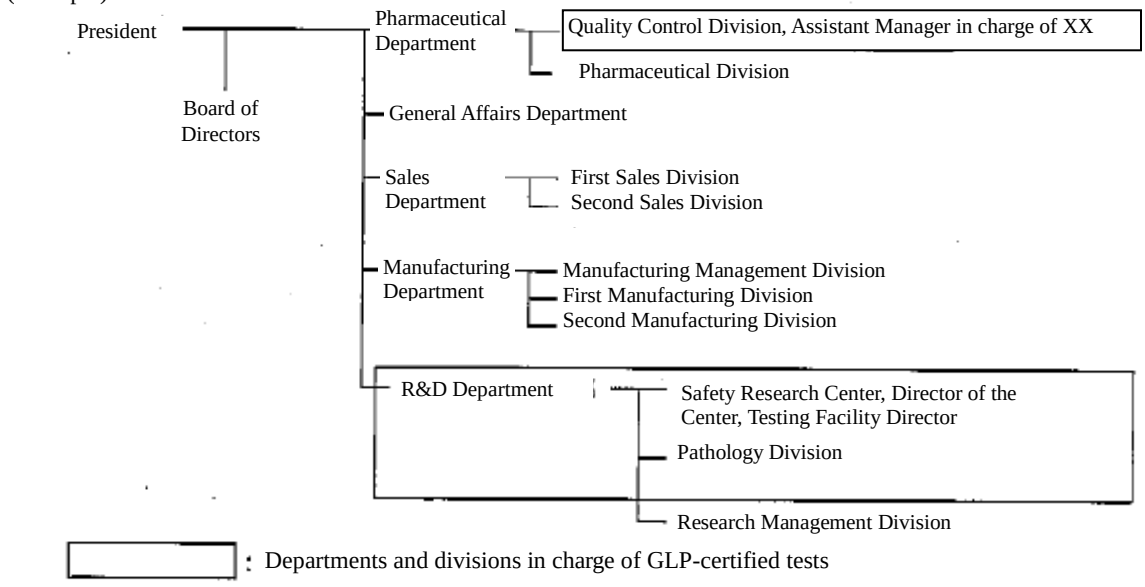
(1) Corporate organization chart

Provide a corporate organization chart that clearly indicates the positions of the GLP-related departments and divisions in the entire organizational structure.

Indicate the GLP-related departments and divisions by putting them in boxes or marking them in some other way.

State the job titles of the key GLP staff members within the corporate hierarchy and the GLP hierarchy, respectively. Write their names if necessary.

(Example)

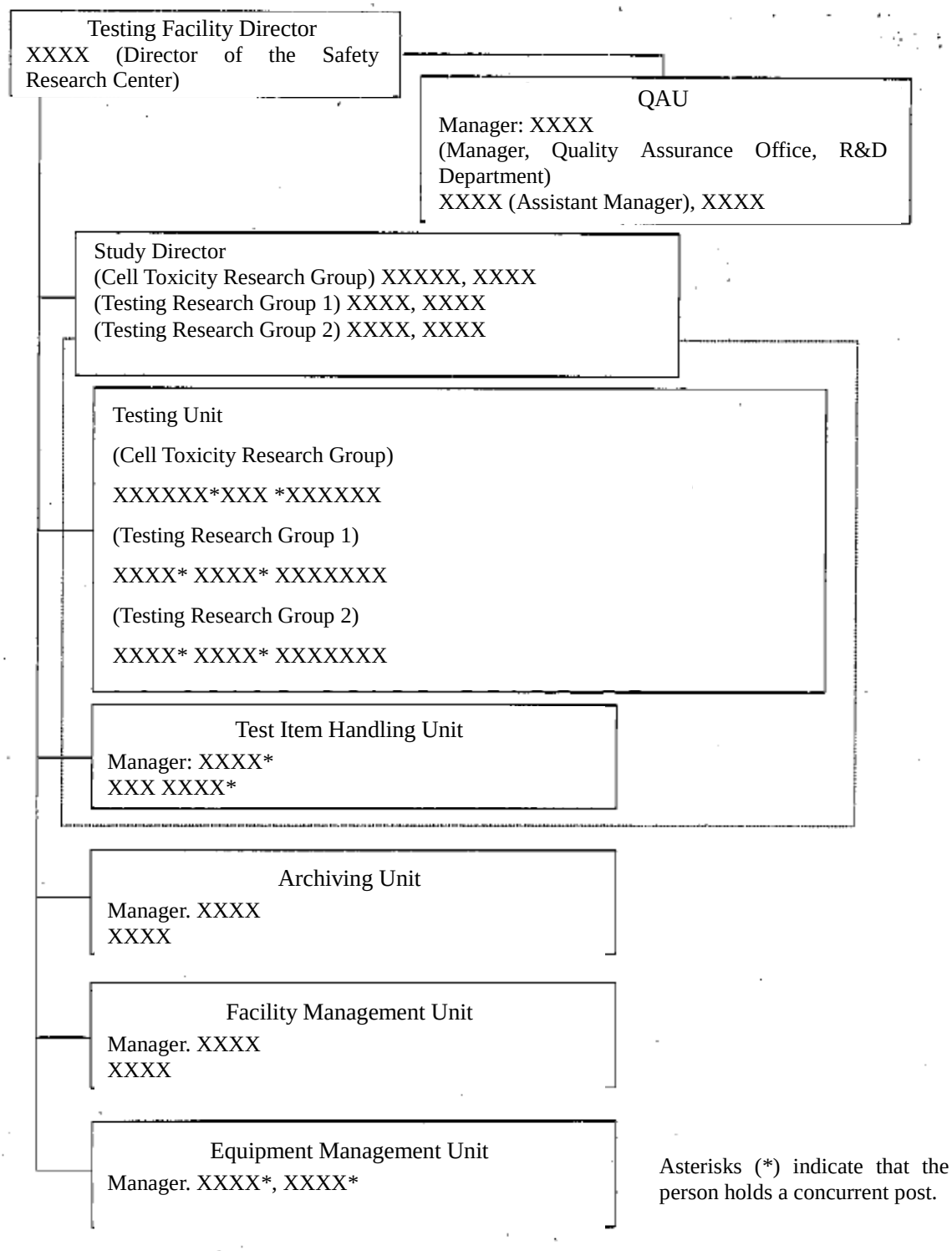


(2) GLP organization chart

Present a chart that describes the roles of the Testing Facility Manager, Study Director, Testing Unit, Quality Assurance Unit (QAU), Archiving Unit, Test Article Handling Unit, Animal Housing Unit, Pathology Unit, System Management Unit, Equipment Management Unit, Facility Management Unit, etc. The chart should also indicate the basic line of command. In addition, write the name of each manager and staff member of each unit.

* The chart should clearly indicate the position of each unit in the entire organizational structure. For example, if the Testing Facility Manager doubles as the director of the Safety Research Center, the indication of the position within the GLP hierarchy should be followed by the position within the corporate hierarchy, e.g. Testing Facility Manager (Director of the Safety Research Center).

(Example)



Asterisks (*) indicate that the person holds a concurrent post.

(3) GLP personnel

A. Total number of GLP personnel (including dispatched workers, temporary staff, employees studying abroad, etc.)

Indicate in parentheses the number of dispatched workers, temporary staff, etc. who are counted in the total number. The name of the staffing agency should also be indicated in the parentheses.

(Example) XX (including XX workers dispatched from YY Staffing Agency)

B. Breakdown of GLP personnel by university department graduated, academic degree, qualification, etc.

Indicate in parentheses the number of dispatched workers, temporary staff, etc. included in the total number. The names of the staffing agencies should also be indicated in the parentheses.

(Example)

	University Department	Degree		Qualification				
		Master	Doctor	Veterinary	Medicine	Pharmacy	Clinical technologist	Others (Note)
Veterinary	3		1	3				
Medicine	1		3*		1			
Pharmacy	1					1		
Agriculture	8	3	2	3				2
Science	5		1					
Engineering	1							
Fishery	1							
Others	0							
Junior college	3						1	
Vocational school	13						1	
High school	12(3)							
Junior high school	2							
Total	47	3	7	6	1	1	2	2

* One person from XX Department, another one from YY Department

The number in parentheses shows the number of workers dispatched from XX Staffing Agency.

(Note) In this section, indicate the number of personnel who have qualifications given by academic societies such as the following:

Pathologist (The Japanese Society of Veterinary Science), Pathologist (The Japanese Society of Toxicologic Pathology), Diplomate of the Japanese Society of Toxicology (The Japanese Society of Toxicology), Japanese Teratology Society-approved Reproductive and Developmental Toxicologist (The Japanese Teratology Society), Laboratory Animal Technician (Japanese Society for Laboratory Animal Resources), QAP (Japan Society of Quality Assurance), Qualified Engineer (Japan Association of Contract Laboratories for Safety Evaluation), Qualified Laboratory Technologist in Experimental Pathology (The Japanese Association of Histotechnology), Qualified Electron Microscopy Technician (The Japanese Society of Microscopy), etc.

C. Breakdown of GLP personnel by unit

State the number of personnel of each unit such as the Quality Assurance Unit (QAU), Testing Unit and Archiving Unit.

(Example)

Unit	Number of personnel	Dispatched workers, temporary staff, etc.	Total
Testing Facility Manager	1		1
Quality Assurance Unit	3		3
Testing Unit	20		20
Archiving Unit	2 (including one staff member who has a concurrent post)		2 (including one staff member who has a concurrent post)
Test Article Handling Unit	2	2	4
Facility Management Unit	2	3	5
Total	29(1)	5	34(1)

* If any of the personnel has a concurrent post, he or she should be counted in the personnel of the unit in which he or she has been most involved. The number of such personnel should be indicated in parentheses.

14. Monitoring of the testing facility by the Testing Facility Manager

Regarding to the responsibilities related to monitor the testing facility among job responsibilities of the Testing Facility Manager specified by GLP regulations, describe how the Manager carries out such monitoring duties (method, frequency, etc.).

(Examples of monitoring duties)

A. Ensure that a sufficient number of qualified personnel, appropriate facilities, equipment and materials are available for the timely and proper conduct of the study;

B. Ensure the maintenance of a record of the qualifications, training, experience and job description for each professional and technical individual;

C. Ensure that personnel clearly understand the functions they are to perform;

D. Ensure that appropriate and technically valid Standard Operating Procedures are established and followed, and approve all original and revised Standard Operating Procedures;

E. Ensure documented approval of the study plan by the Study Director;

F. Ensure that the Study Director has made the approved study plan available to the Quality Assurance personnel;

G. Ensure the maintenance of an historical file of all Standard Operating Procedures;

H. Ensure the maintenance of a master schedule;

I. Ensure that testing facility supplies meet requirements appropriate to their use in a study;

J. Ensure that test and control articles are appropriately characterized;

K. Ensure, in the event of a multi-site study, that, if needed, a Principal Investigator is designated, who is appropriately trained, qualified and experienced to supervise the delegated phase(s) of the study.

L. Ensure for a multi-site study that clear lines of communication exist between the Study Director, Principal Investigator(s) (if appointed), the Quality Assurance Unit(s) and study personnel;

15. Criteria for selecting study directors (appointment procedure)

Indicate the criteria for selecting Study Directors, such as required qualifications, and describe the selection procedure.

(Example)

For each animal test, the Testing Facility Manager shall appoint a Study Director from among those who have at least 10 years of experience in animal toxicity study or who have sufficient skills to become Study Director.

For each XX study, the Testing Facility Manager shall appoint a Study Director from among those who have at least 2 years of experience in XX study or who have sufficient skills to become Study Directors.

16. Education and training programs recently offered to personnel

Classify the education and training programs on GLP regulations and GLP applicable studies into the following five groups, from A to E, and briefly describe each program.

A. New employee education

B. On-the-job training (OJT)

C. In-house training (education and training offered within the company, including by guest lecturers)

D. Out-of-house training

E. Participation in academic meetings, etc.

List the education and training programs offered in the last three years, with details such as the contents (title) and the trainees (participants) of each program.

(Example)

Outline of education and training programs

A. New employee education

1. GLP education to new employees

GLP education is given to new employees in early April, based on the GLP education principle.

C. In-house training

1. GLP education, computer training

This in-house training is given to new employees, newly assigned personnel, etc. to deepen their understanding of the GLP system and safety.

E. Academic meetings, etc.

1. Various academic meetings, etc.

Employees are allowed to attend academic meetings to maintain and enhance their expertise.

Education and training programs offered in the last year

A. New employee education

1. GLP education

Date: April 2-14, XXXX

Lecturer: XXXX Trainees: XXXX XXXX

B. In-house training

1. GLP education, computer training

Date: July 12, XXXX

Lecturer: XXXX Trainees: XXXX (manager), XXXX (in charge of XX), Total number of trainees: XX

E. Academic meetings, etc.

The Japanese Society of XX, Date: November 14-17, XXXX

Participants: XX XX XX XX

17. Testing experience of Study Directors

State the total number of studies that each Study Director has conducted. The number of studies that he or she has supervised as a Study Director shall be indicated in parentheses.

If the number is 10 or larger, it is acceptable to state an approximate number, e.g. “about X.”

(Example)

Name	Total number of studies conducted (number of studies as a Study Director)
XXXX	XX study : 38 (26) YY study : 8 (6) ZZ study : 5 (3)
XXXX	XXX study : 58 (42)

	YYY study : 4 (1)

18. Job responsibilities, names, job titles, qualifications, job histories, research careers, academic society membership, etc. of the Testing Facility Manager and other major personnel

Provide detailed information about each person listed from A to I below. The information should cover his or her job responsibilities, name, date of birth, job title, academic degree(s), qualification(s), license(s), job history, research career, training records, and membership in academic societies and other organizations. In addition, provide a list of his or her research papers and presentations.

A. Testing Facility Manager
B. Study Director (information should be provided for all the candidates)
C. Archiving manager
D. Test article manager (if any)
E. Animal housing manager (if any)
F. Pathology manager (if any) and personnel in charge of histopathological study (if any)
G. All the staff members of the Quality Assurance Unit
H. Equipment manager (if any)
I. Other managers (if any)

*1. Information on current managers should be provided.
*2. Regarding G, clearly describe the roles of each QAU staff member if they each have specific job responsibilities.
*3. In the section on research career and training records, describe the outline of the research projects, experience of GLP study (if any), and achievements as a researcher (research papers and presentations, etc.) at the organization or university to which the manager belonged at that time. Only the research papers and presentations related to GLP applicable studies should be mentioned. If there are five or more papers in each field of study (e.g. general toxicity, pathology, etc.), list five major papers in each field and state the number of papers remaining (e.g. XX more papers).
*4. The “Archiving manager” referred to in C means “Materials and data storage manager” under the Law on Chemical Evaluation and the Law on Industrial Safety, “Materials storage manager” under the Law on Agricultural Chemicals Control and the Law on Feed Safety, and “Materials storing facility manager” under the Pharmaceutical Affairs Law (pharmaceuticals for animals) and the Law on PMDA.
*5. The information on H should cover the names of major pieces of equipment that the manager is

in charge of (if a manager is appointed for each study field and each type of facility, state as such), and the name and job title of the manager.

The applicant may wait until Section 23 to provide a list of the names of major pieces of equipment that the manager is in charge of. In that case, state as such.

(Example)

Job responsibilities	Study Director (XX XX,XXXX to the present)
Name	XXXX
Date of birth	X XX XXXX
Job title	Group Leader, Pathology Research Group, Safety Research Department
Degrees, qualifications, licenses	May 1977 Licensed as a pharmacist (License No. XX) March 1979 Obtained a bachelor's degree in Pharmacy March 1993 Certified as a pathologist by the Japanese Society of Toxicologic Pathology (Certification No. XX) April 1993 Certified as a pathologist by the Japanese Society of Veterinary Science (Certification No. XX)
Job history	1977 Graduated from Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Science, XX University 1979 Obtained a master's degree from Pharmaceutical Research Department, XX University Graduate School April 1979-March 1985 Worked as a researcher at First Research Division G, Safety Research Center, XX Pharmaceutical Co., Ltd. April 1985-March 1993 Worked as a researcher at Pathology Research Division G, Safety Research Center, XX Pharmaceutical Co., Ltd. April 1993-Today Working as a senior researcher at Pathology Research Division G, Safety Research Center, XX Pharmaceutical Co., Ltd.
Research career and training record	Pathology April 1982-Today XX Pharmaceutical Co., Ltd.: Papers (1)-(3) April 1983-March 1985 Student of Pathology Course X, XX University: Papers (4)-(5) XX study April 1979-March 1985 XX Pharmaceutical Co., Ltd.: Papers (6)-(10) YY study April 1981-Today XX Pharmaceutical Co., Ltd.: Papers (10)-(15)
Academic societies	The Japanese Society of Pathology, The Japanese Cancer Association, The Japanese Society of Toxicologic Pathology
Related organizations	The Japanese College of Veterinary Pathologists (membership)

(* Attach a list of research papers and presentations.)

19. Quality Assurance Unit (QAU)

Indicate whether or not the Quality Assurance Unit (QAU) is a permanent section of the GLP organization.

(Example) The QAU is a permanent section.

20. Major activities of GLP-related departments and divisions

Briefly describe all the activities conducted at the testing facility. If any activities other than GLP-related activities (non-GLP-related activities) are conducted at the facility, outline those activities as well.

(Example)

XX study

YY study

ZZ study

(CC study)

21. Animal housing capacity of the Testing Unit

Indicate the animal housing capacity of each building. If a building houses different species of animals simultaneously or alternately, clearly state this.

If there is a building with no animal housing capacity, state this.

(Example)

Building	Room No.	Number of rooms	Grade	Animal species	Number of housing units (cages or tanks)	Maximum capacity (size)
Building 1	101-105	5	Barrier	Mice	30 x 5 cages	1,500
	201-204	4	Barrier	Mice	30 x 4 cages	600
	301-303	3	Barrier	Rats	25 x 3 cages	375
Building 2	201-205 * Either rabbits or guinea pigs are housed depending on the study type	6	Conventional	Rabbits Guinea pigs	50 x 6 cages 25 x 6 cages	300 450
	207-211	5	Conventional	Rats	30 x 5 cages	750
Cow barn	101	1	Conventional	Cows	6 stalls	6
Fish medical ward	206	1	Conventional	Red sea bream	0.3t tank x 10	2,000 (15g)

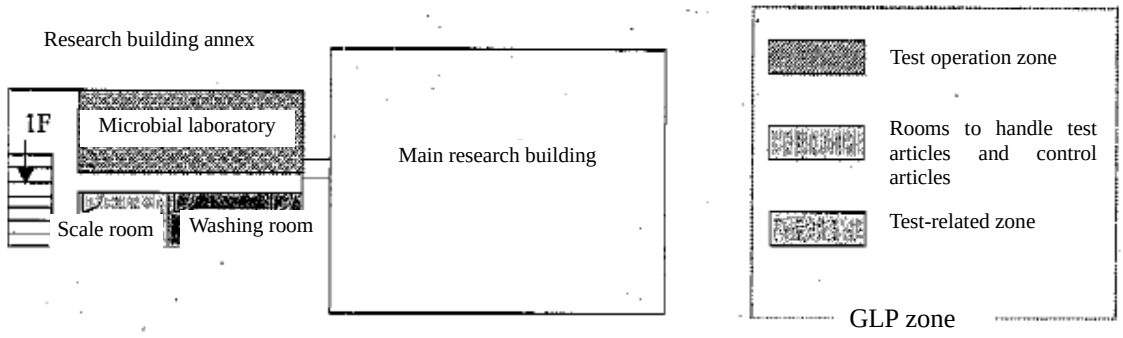
22. Floor plans, circulation diagrams and air conditioning diagrams for each operation zone of the safety (toxicity) study unit

(1) Floor plan of each operation zone

A. Provide the floor plan of each animal housing zone or any other operation zone, indicating the locations of the major facilities in the room. Differentiate the GLP zone from the non-GLP zone and write the name (purpose) of each room. Attach photographs of the major instruments, as necessary.

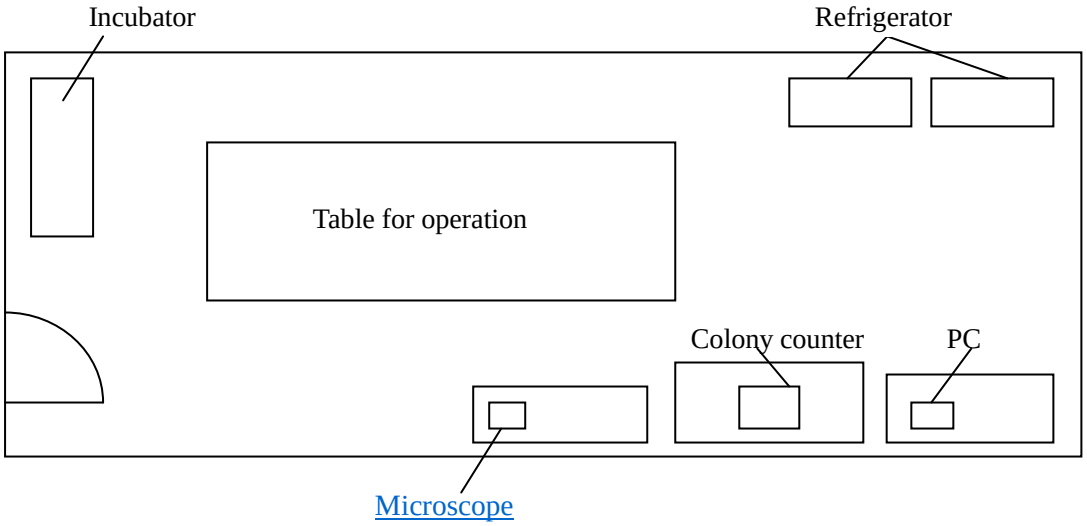
* Clearly indicate the boundaries of each barrier animal room by using bold lines and letters.

(Example)



a) Zone for operating study

Microbe laboratory



b) Zone for handling test item and control item

.....

(2) Circulation diagrams

Prepare diagrams indicating the following circulation patterns:

A. the route of animal subjects from entry to exit (including the anatomy room);

B. the route of animal feed (basic feed), equipment, etc. from entry to exit;

C. the exit route of waste (filthy matter) from the housing room;

D. the route of staff from entry to exit;

E. the circulation route of test articles (or mixtures) and positive control articles; and

F. the flow chart of waste (including wastewater).

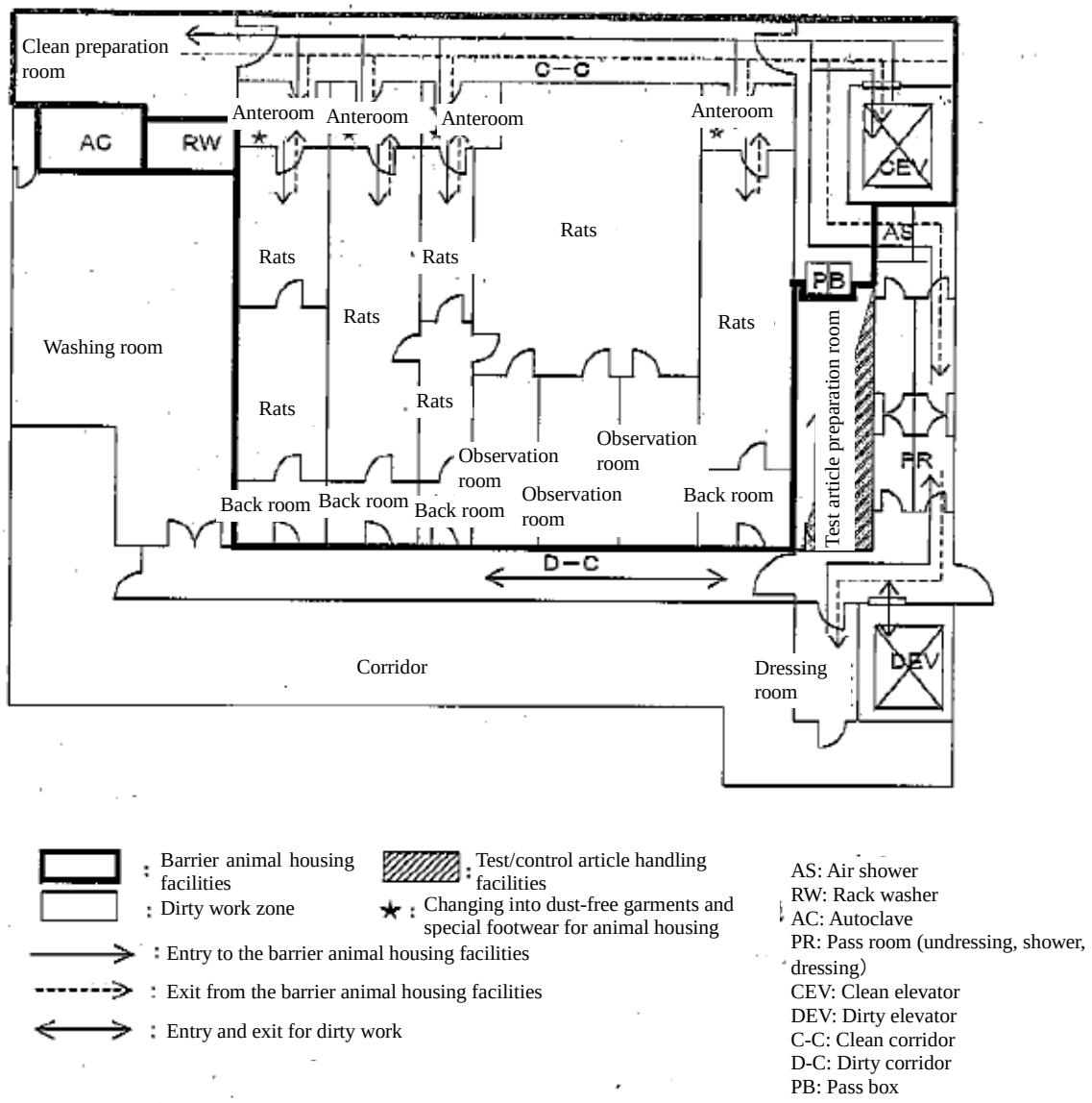
*1. Use colors or other techniques to make the diagrams easy to understand.

*2. Use bold lines or other techniques to clearly indicate the boundaries of each barrier animal housing room.

*3. Regarding D, indicate the routes for clean work and dirty work respectively.

*4. The routes specified in A to D shall be indicated in the animal housing zone diagrams (including any related facilities outside the animal housing zone).

(Example) Route of staff from entrance to exit in an animal housing room



(3) Air conditioning diagrams

Include the following information A and B in the diagrams.

A. Diagram of the air conditioning of the facilities

B. Diagram of the air flow in the barrier system

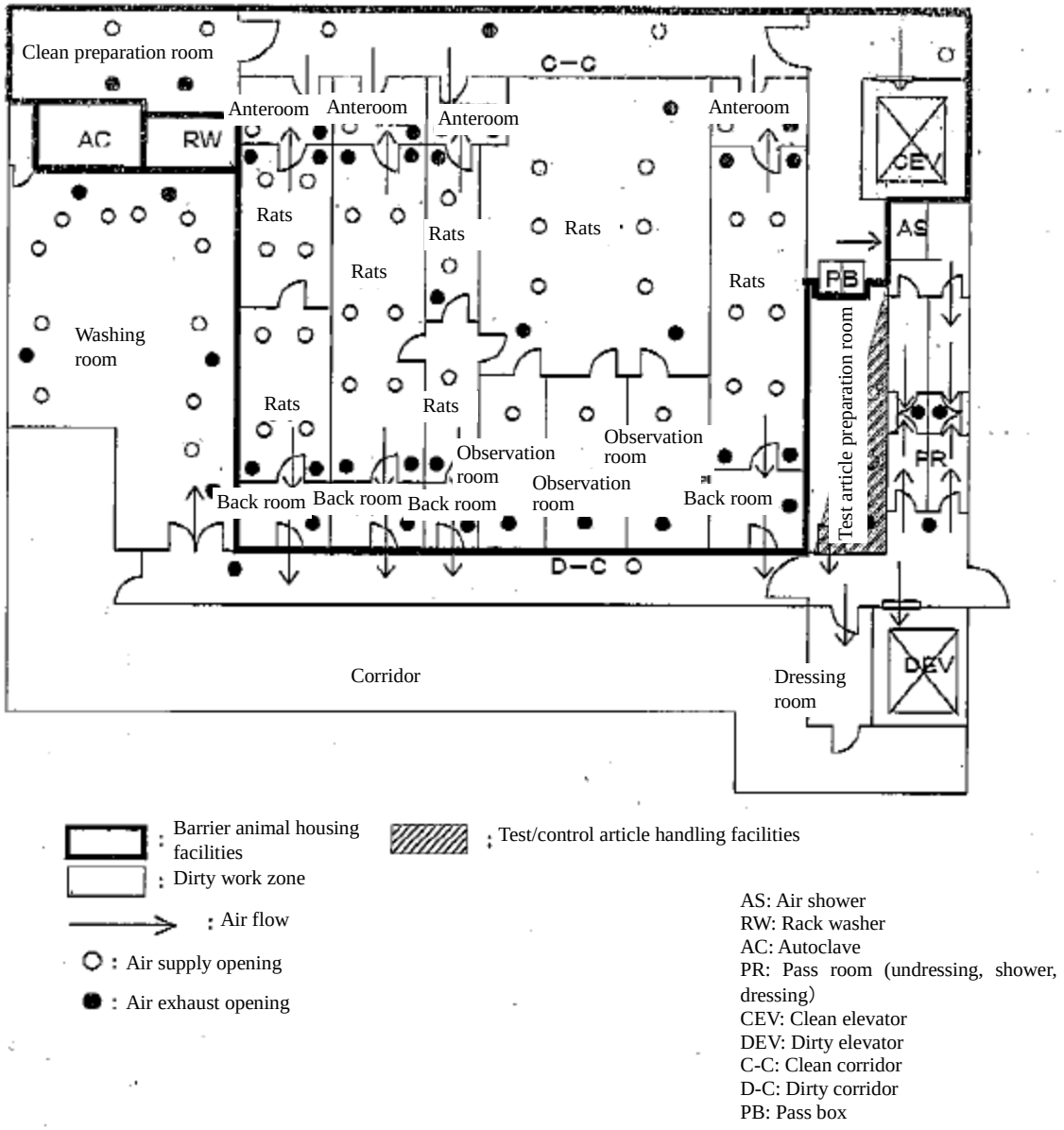
*1. Use colors or other techniques to make the diagrams easy to understand.

*2. Indicate the types of air filters.

*3. Indicate the location(s) of heat exchange, if any, between exhaust and supply air.

*4. Indicate air supply and exhaust openings.

(Example) Diagram of the air conditioning of the facilities



23. Handling and disposal of waste

Describe how waste materials are handled and disposed of.

(Example)

(1) Animal carcasses are:

1. Put it in a plastic bag and then in a special container, which will be sealed and stored in a freezer;

2. Periodically (once a week) collected by a waste disposer (XX Co., Ltd., Governor's approval No.

XX); and

3. Transported by the disposer by XX, incinerated at XX and buried in XX.

(2) Disposal of wastewater, etc.

24. Names, numbers, models, etc. of major facilities and equipment used for study (facilities and equipment)

Indicate the names, numbers, models, etc. of major facilities and equipment used for study. Such information shall be provided for each installation location.

* The information shall cover major computers for data analysis, major equipment for environment control of facilities, etc.

* State the magnification of microscopes and the accuracy of scales in the remarks column, respectively (as necessary).

(Example)

Installation site	Name	Number	Manufacturer	Model	Purchase date	Remarks
XX	XX	1	XX	XX-XX	X/X/X	XXX

25. Animal housing facilities

(1) Animal housing conditions

State the temperature, water temperature (for fish), humidity, lighting (lighting intensity), lighting hours, noise, cleanliness (dust, microbes, etc.), ventilation frequency, differential pressure, etc. Indicate the housing conditions of the barrier area separately from those of the conventional area if the two differ from each other in terms of housing conditions.

(Example)

Items		Barrier area	Conventional area
Temperature	Management standard	21-25 C	
	Allowable range	20-26 C	
Humidity (relative humidity)	Management standard	45-65 %	
	Allowable range	35-75%	
Lighting (lighting intensity)	Management standard	350 lux or higher	
Noise	Management standard	55dB or lower	
Cleanliness (airborne bacteria)	Management standard	4 colonies or less/plate	40 colonies or less/plate
Differential pressure	Management standard	1 mmH_2O or higher	
Ventilation frequency	Management standard	20 times or more/hour	15 times or more/hour
	Allowable range	12 times or more/hour	

(2) Sources and update frequency of analytical data on feed, water and bedding

Indicate sources and update frequency of analytical data on each type of feed, water and bedding.

(Example)

Feed

Nutritional analysis (data is obtained from the supplier for each lot)

Toxic substance microanalysis (data is obtained from the supplier for each lot)

Microbial testing (data is obtained from the supplier for each lot; in addition, self-performed analysis is conducted once a year)

Water

Water testing (the test is conducted by an outside company XX times per year)

Bedding

Toxic substance microanalysis (data is obtained from the supplier about every ZZ months)

(3) Microbial monitoring of animal housing rooms, etc.

If microbial monitoring such as airborne bacteria count is conducted, indicate the measurement sites (mark the locations of petri dishes) in the floor plan of the animal housing room, measurement frequency, allowable microbial contamination levels, etc.

26. Environmental control of important zones and the monitoring procedures

Regarding the important zones listed as A to E below, where the temperature, humidity, differential pressure, etc. are controlled, describe the methods of environmental control, the monitoring procedures and the measures to be taken when a problem occurs.

A. Animal housing zone

B. Animal supplies storage zone

C. Test article storage zone

D. Study operation zone

E. Special study zones to handle chemical hazards, biohazards, etc.

* Regarding the measures taken when a problem occurs, provide the following information based on the facility rules and SOP.

- Reporting from the detector (how a staff member can detect a problem, monitoring system, etc.)
- How and to whom should the detector report? (Emergency reporting system (communication network), etc.)
- Who should make a decision based on the report and handle the problem?

(Example)

A central air conditioning monitoring system installed in the central control room monitors and controls, around the clock, the temperature and humidity of the animal housing rooms, archiving rooms and low-temperature laboratories.

If any problem occurs in XX, it will be immediately notified to the central control room and ---

27. Washing and disinfection procedures

(1) Use of detergents and disinfectants

Indicate the use of detergents and disinfectants for each item.

Describe the washing and disinfection procedures.

(Example)

Procedure Items	Replacement frequency/week	Washing	Disinfection	Sterilization	Cleaning	Rinsing after disinfection
a) Cages						
b) Feeders						
c) Water bottles						
d) Counters						
f) Case cards (label holders)						
g) Automatic feeders						
h) Automatic water feeders						
i) Water tanks						
j) Feed containers						
(in animal housing rooms)						
k) Floors						
l) Ceilings						
m) Walls						
n) Drainage						
o) Lamps						

(2) Use of insecticides

Describe the use of insecticides.

(Example)

Insecticides are used for each floor once a year. The last use was on X XX, XXXX.

28. Management of animals and animal care

(1) Procedure for receipt, quarantine and animal care

Briefly describe the following points A to F. Description may be given for each animal species.

A. Information on animals received to the testing facility (producers (in-house production, commissioned production, outside producers, etc.), animal types (SPF animals, germ-free animals, etc.), use of vaccines, anthelmintics, antifoulants and other chemical agents on animals, availability of records of microbial monitoring, transport and receipt of animals)

B. Procedure for receiving animals

C. Receipt inspection (state whether the following checks are performed: quantity check, sex check, body weight measurement, appearance check and records check)

D. Quarantine and acclimatization (period of quarantine and acclimatization, items examined in microbial tests (protozoa, parasites, bacteria, etc.), clinical tests, qualifications of the person in charge of health evaluation, items covered by animal care records (findings of microbial tests, body weight records, etc.))

E. Animal care method

F. Use of vaccines, anthelmintics, insecticides, antifoulants and other chemical agents on animals

(Example)

(Rats)

A. Information on animals received by the testing facility

- Producer of animals	Outside producer
- Type of animals	SPF animals
- Use of chemical agents on animals	None
- Records of microbial monitoring	Available
- Records of transport of animals	None
- Records of receipt	Available

B. Procedure for receiving animals Separate rooms are used to receive, quarantine and house animals.

C. Receipt inspection

- Quantity check	Conducted
- Sex check	Conducted
- Body weight measurement	Conducted
- Appearance check	Conducted
- Records check	Conducted

D. Quarantine and acclimatization

- Period of quarantine and acclimatization XX days
- Items examined in microbial tests Parasites, bacteria and viruses
- Clinical tests None
- Qualifications of person in charge of health evaluation Animal care manager (veterinarian)
- Items covered by animal care records General checkup, body weight

E. Animal care method Barrier system

F. Use of chemical agents on animals None

(2) Handling of diseased animals and animals presenting disease-like symptoms

Briefly describe the in-house rules, if any, on how to handle diseased animals and animals presenting disease-like symptoms.

If you have handled such animals since the last inspection (in the case of first-time inspection, if you have ever handled such animals), provide information on the following points A to E.

A. Date of occurrence of the incident

B. Species and strain of animals

C. Type of study for which the animals had been used

D. Details

(a) The disease or symptoms were found in XX out of XXX animals (or in XX out of XXX monitored animals).

(b) The disease or symptoms were found on the Xth day of a XX-day administration study or found in monitored animals on the Xth day from the first administration.

(c) How was the disease or symptoms detected? (Detected by a monitor test, detected by a general observation, etc.)

(d) Was any other study conducted in the same housing room?

(e) Was any other study conducted in the same housing zone?

E. Measures

(a) Examination and treatment of such animals

(b) Checking of infection of other animals in the same housing room or zone

(c) Continuation or suspension of the study mentioned in D (d) and (e)

(d) Availability of raw data (animal care records, general study records, etc.) concerning the incident or availability of any document recording the incident

(e) If the study was continued, indicate whether this incident was mentioned in the final report

(Example)

Any researcher who detects a diseased animal or an animal with disease-like symptoms shall make a record in a prescribed format, report the incident to the Study Director, and isolate or destroy the animal in the isolation room in accordance with the instructions of the Study Director.

If the animal is to be destroyed, it shall be euthanized upon the Study Director's approval. The incident shall be recorded and filed in a prescribed format.

(3) Management of feed, water, animal care instruments, detergents, etc.

Briefly describe the following points, A to E, concerning the management of feed, water, animal care instruments, detergents, etc.

A. Acceptable quality levels of feed and water

(whether such levels are specified in the facility rules)

B. Feed

(manufacturer, type of feed (for each species), form of feed, site of analysis, storage conditions of feed, availability of records)

C. Water

(availability of tap water specified in the Water Supply Act, availability of an in-house water pumping system or water receiving tank, type of toxic metal removal equipment, type of disinfecting or sterilizing equipment, microbial monitoring of watering bottles, replacement frequency of watering equipment such as watering bottles, site of analysis, availability of records)

D. Animal care equipment and instruments

(availability of facilities for washing, disinfecting and sterilizing animal care equipment and instruments, storage methods of animal care equipment and instruments)

E. Use of any detergent or insecticide negatively affecting the studies since the last inspection

(if used, instructions given by the Study Director, reasons for use, type of detergent or insecticide, range of use, method of use, amount of detergent or insecticide used, availability of records)

(Example)

A. Acceptable quality levels of feed and water

The levels are specified in SOP XXXX.

B. Feed

(Rats and mice)

Feed maker	XXXX Co., Ltd.
Type of feed	XX-X
Form of feed	Solid powder

- Site of analysis Analysis results obtained from the feed maker.
- Feed storage conditions Same as the animal care conditions. The maximum storage period is six months from the manufacturing date.
- Records Available

C. Water

- Availability of tap water specified in the Water Supply Act Available
- In-house water pumping system None
- Water receiving tank Available
- Type of toxic metal removal equipment None
- Type of disinfecting or sterilizing equipment 5 μ m membrane filter
- Microbial monitoring of watering bottles None
- Replacement frequency of watering equipment such as watering bottles Once every xx months
- Site of analysis Commissioned to XX Testing Laboratory
- Records Available

D. Animal care equipment and instruments

- Animal care equipment and instruments Facilities for washing and disinfection
- Storage methods of animal care equipment and instruments Stored in an instrument storeroom

E. Use of any detergent or insecticide negatively affecting the studies

None

29. Master schedule

Attach the copy of master schedule in the month of creating this document or the one month before creating this document.

30. Standard Operating Procedures (SOPs)

(1) Copy of SOPs and formats prescribed in SOPs

Submit copy of SOPs and formats prescribed in SOPs concerning the below procedures.

1) For creating study plan (include formats)
2) For creating final report (include formats)
3) For conducting studies, judging study results and managing the case appearing unexpected values
4) For archive

(2) Preparation, revision, abolishment, etc. of SOPs

(Example)

1. Preparation of SOPs

SOPs shall be approved (prepared) by the Testing Facility Manager.

2. Revision of SOPs

Any staff member who finds it necessary to revise SOPs, --

3. Abolishment of SOPs

Any staff member who finds SOPs no longer necessary, --

(3) List of the titles of SOPs

* Provide a list showing the total number, serial numbers (symbols) and titles of SOPs.

If SOPS are numbered (marked) in a systematic way, explain the numbering system.

(Example)

Each SOP number contains two sets of letters as shown in the following comprehensive list. The letters are followed by a serial number.

SOP/SOP/000 Standard Operating Procedures

SOP/QAU/000 Quality Assurance Unit (QAU)

SOP/REP/000 Final Report

…

List of titles

Standard Operating Procedures

SOP/SOP/001 Preparation of Standard Operating Procedures

SOP/SOP/002 Formats of Standard Operating Procedures

Quality Assurance Unit (QAU)

SOP/QAU/001 Work responsibilities of Quality Assurance Unit (QAU)

31. Flowchart of safety (toxicity) studies

Present a flowchart of an entire study procedure, from the study planning phase to the completion of the study.

A. Discussion with a sponsor

(a) Request for a study from the sponsor

(b) Sponsor's approval for a protocol

(c) Submission of the final report to the sponsor

B. Testing Facility Manager

(a) Appointment of a Study Director and a Quality Assurance Unit (QAU) manager in charge of the study

(b) Preparation of SOPs

(c) Approval or endorsement of a protocol

(d) Submission of the final report from the Study Director

C. Quality Assurance Unit (QAU)

(a) Appointment of QAU personnel specifically for the study

(b) Submission of improvement recommendations and an inspection report to the Testing Facility Manager

(c) Submission of improvement recommendations and an inspection report to the Study Director

D. Flow of study procedure

(a) Preparation of a protocol

(b) Signing by the Study Director

(c) Approval or endorsement by the Testing Facility Manager (and the sponsor who commissioned the study), inspection by the Quality Assurance Unit (QAU), etc.

E. Procedure for handling test and control articles

(a) Request for analysis

(b) Implementation of analysis

(c) Receipt of analysis records

(d) Order placement, receipt, storage and return of test and control articles

F. Final report

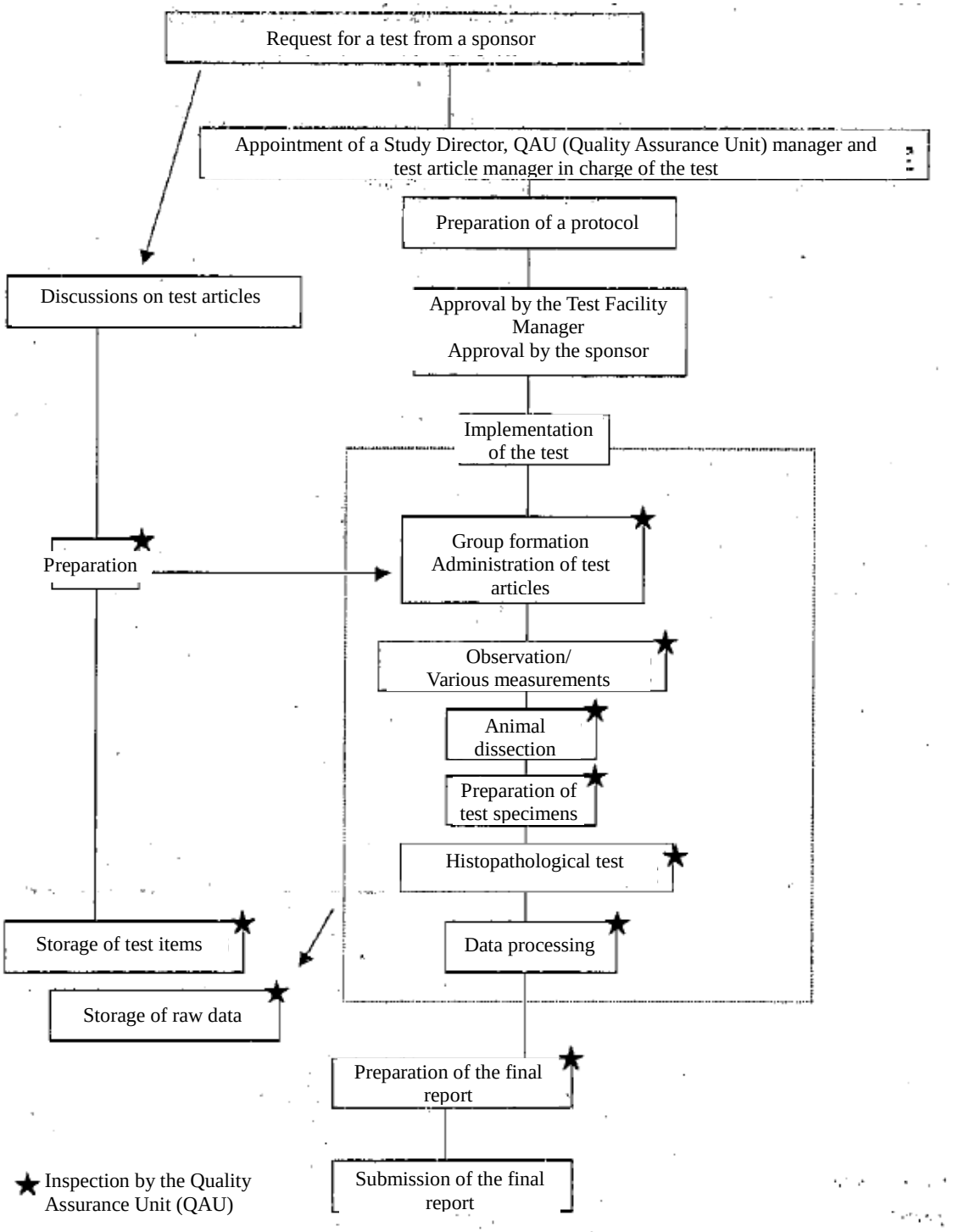
(a) Signing by the Study Director

(b) Inspection by the Quality Assurance Unit (QAU)

G. Archiving procedure

H. Others

(Example) Flowchart of safety (toxicity) studies



32. Outline of computer system

If a computer system is used to process study data, describe what it is used for (data collection, preparation of tables and charts attached to the final report, statistical calculation, etc.) and how it is used. State the definition of raw data and the procedures for modification and correction of raw data.

Regardless of how raw data is defined, provide information on the following points, A to E, concerning use of the computer system.

A. Patterns of computer use

B. Names of the system and system developer

C. If a commercially-marketed system was put to use after partial alteration, describe how and in which part the alteration was made.

D. Configuration of the system

E. Method and frequency of system validation

(a) Use of computers in studies

In the flowchart of a safety (toxicity) study, indicate when computers are used.

(b) Hardware configuration

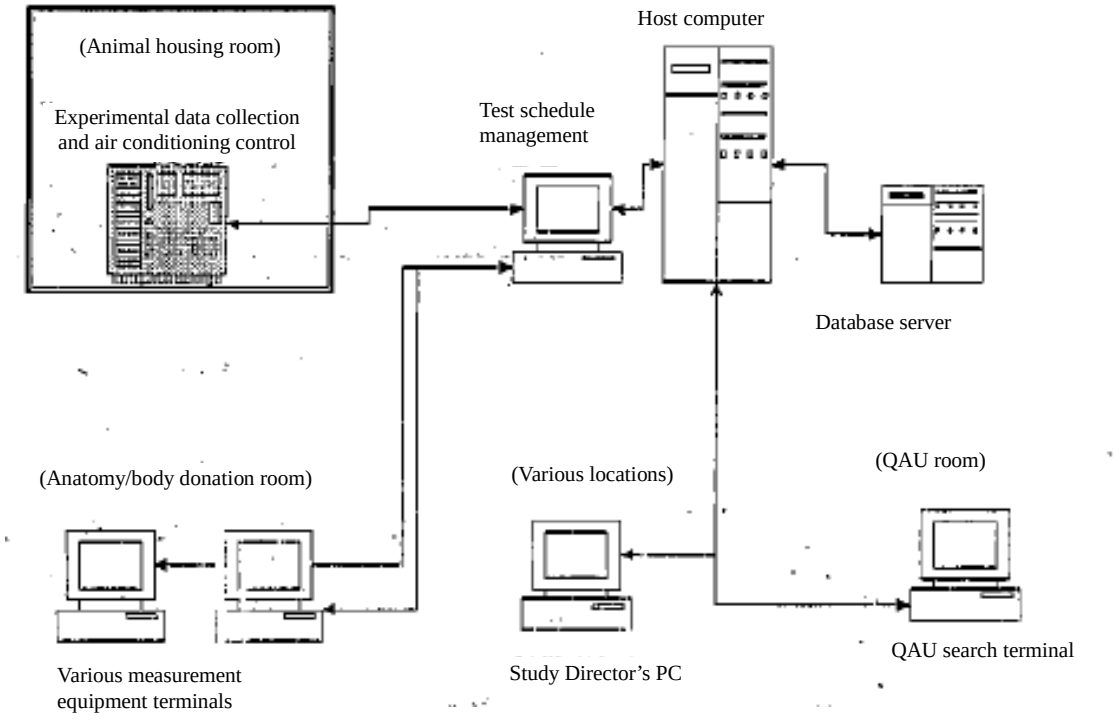
Indicate the host computer, LAN, data collection terminals, connectors, etc.

(c) Software configuration

Indicate the system performance and the studies and inspection for which the system is used.

(Example)

A. On-line computer system



B. Standalone computers

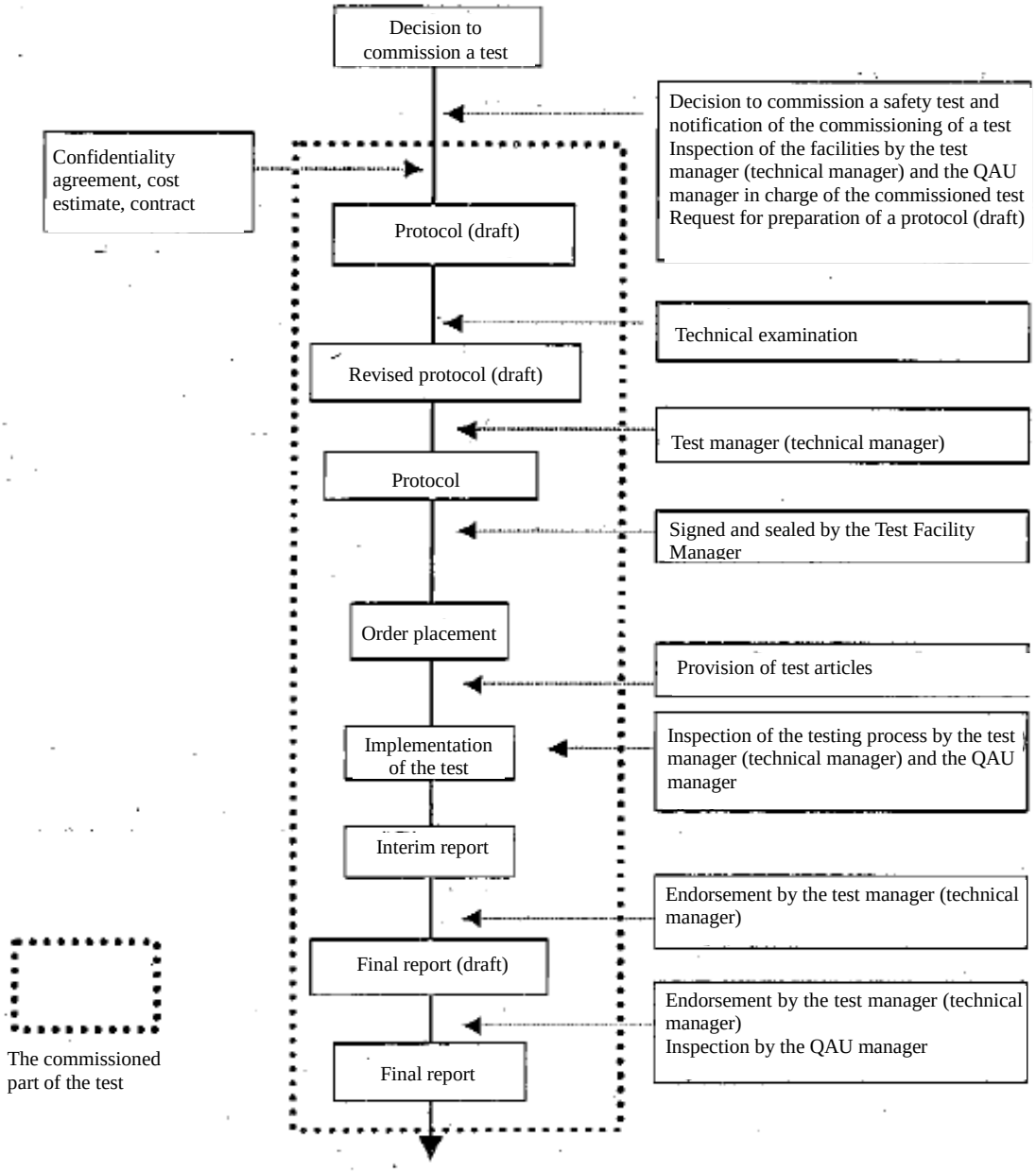
(1) XX measurement system: XXX made by YYY is used to measure the body weights of test animals in the YY study. The system was installed in XXXX in YYY room.

33. Commissioning of studies to outside organizations

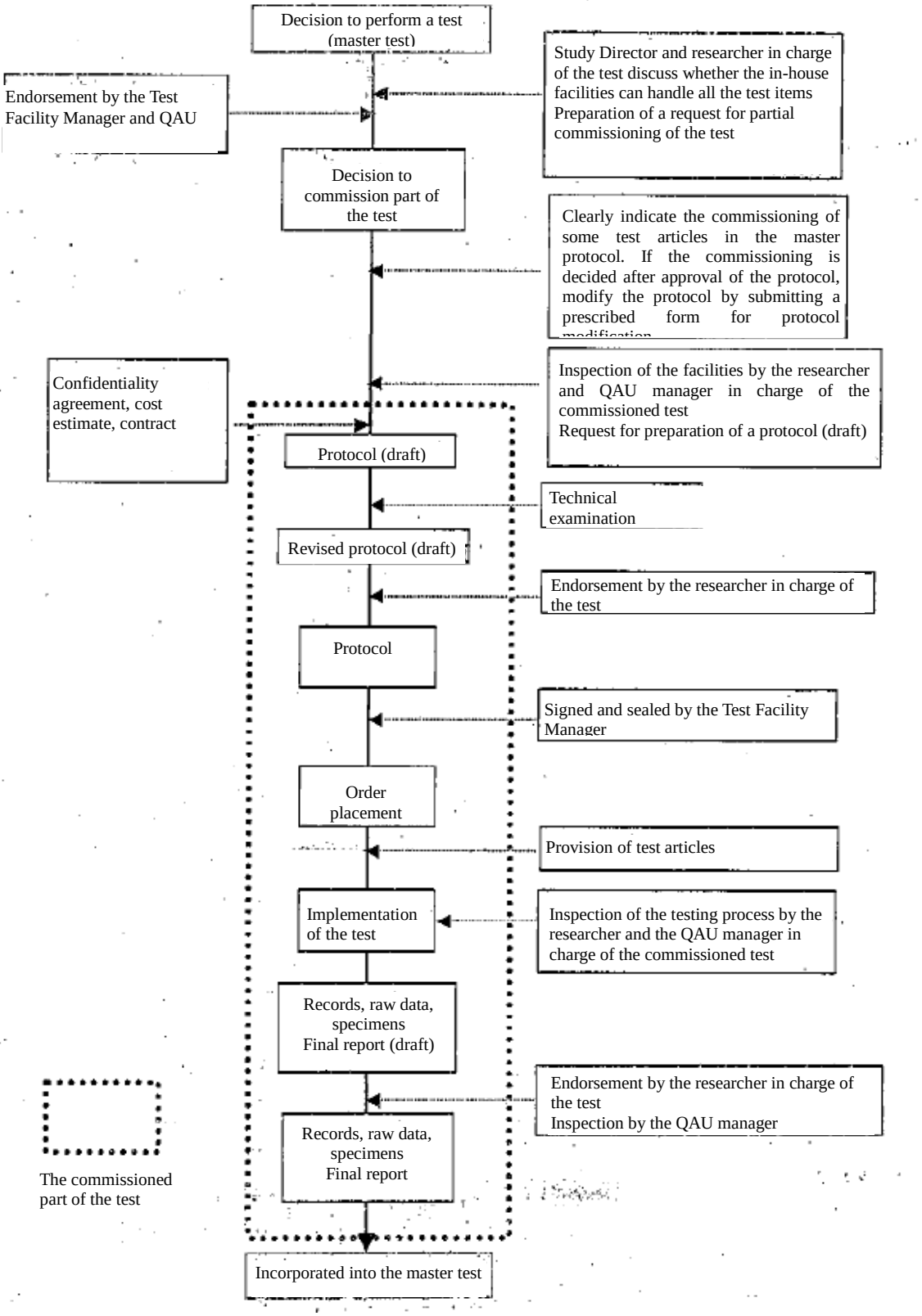
Provide a flowchart of the procedure for commissioning of a study (delivery of specimens, handling of test articles, QAU inspection, etc.). If studies are commissioned to more than one organization, present a flowchart of the commissioning procedure adopted with the organization to which studies are most frequently commissioned.

(Example)

A. Commissioning of an entire study



B. Commissioning of part of the study items



34. Recommendations made in the last GLP inspection and recent improvements

State the recommendations made in the past GLP inspection. Describe in detail any improvements made in response to each recommendation.