Tentative translation ver. 2.9 (as of 5 September 2005)[1]

MHW Ministerial Ordinance No. 2, 1961

Amended by:
MHW Ministerial Ordinance No.47, 1964;
MHW Ministerial Ordinance No.21, 1968;
MHW Ministerial Ordinance No.32, 1980;
MHW Ministerial Ordinance No.35, 1980;
MHW Ministerial Ordinance No.39, 1983;
MHW Ministerial Ordinance No.45, 1985;
MHW Ministerial Ordinance No.29, 1987;
MHW Ministerial Ordinance No. 2, 1989;
MHW Ministerial Ordinance No.30, 1990;
MHW Ministerial Ordinance No. 4, 1994;
MHW Ministerial Ordinance No.41, 1995;
MHW Ministerial Ordinance No.29, 1997;
MHW Ministerial Ordinance No.71, 1997;
MHW Ministerial Ordinance No.40, 1998;
MHW Ministerial Ordinance No.18, 1999;
MHW Ministerial Ordinance No.57, 1999;
MHW Ministerial Ordinance No.103, 1999;
MHW Ministerial Ordinance No. 99, 2000;
MHW Ministerial Ordinance No.127, 2000;
MHW Ministerial Ordinance No.150, 2000;
MHLW Ministerial Ordinance No.49, 2001;
MHLW Ministerial Ordinance No.54, 2001;
MHLW Ministerial Ordinance No.92, 2003;
MHLW Ministerial Ordinance No.116, 2004;
MHLW Ministerial Ordinance No.180, 2004; and

Supplementary Provisions

(Enforcement Date)

Article 1 This Ministerial Ordinance shall come into effect on 1 April 2005.

(Transitional Measures)

Article 2 For 2 years from the date of enforcement of this Ministerial Ordinance, the provision of Chapter 2 revised by this Ministerial Ordinance may not apply to the foreign manufacturer.

MHLW Ministerial Ordinance No.73, 2005.

Regulations for Buildings and Facilities of Pharmacies, etc.

CONTENTS

[1] **Note/ This is a tentative translation of afore-mentioned Ordinance in English which is not an authentic and not formally autholised by Ministry of Health, Labour and Welfare of Japan.**

Chapter 1 Pharmacies, Distributors of Drugs, and Distributors, Leasers and Repairers of Medical Devices

(Buildings and Facilities of Pharmacies)

Article 1 The buildings and facilities of the pharmacy shall meet the following requirements.

(1) To be well ventilated and clean,

(2) To be distinctly segregated from the living quarters and unsanitary areas,

(3) To be ensured that the area is at least 19.8 square meters and to allow the appropriate operations of the pharmacy,

(4) To be provided with the lighting of at least 60 luxes in the areas where the drugs are routinely displayed or delivered, and the lighting of at least 120 luxes on the dispensing workbenches,

(5) To be provided with the dispensing room which meets the following requirements,

a. Being ensured that the area of the dispensing room is at least 6.6 square meters, and

b. Being ensured that the ceilings and floor of the dispensing room are made of wood, concrete or equivalent materials.

(6) To be provided with the facilities for storing in a cooled and/or dark condition,

(7) To be provided with the storage facilities that can be locked with locks,

(8) To be provided with the following facilities and equipment required for the dispensing,

a. Liquid measuring equipment (those of which capacity are 20 cc and 200 cc),

b. Thermometers (100° C),

c. Water baths,

d. Dispensing workbenches,

e. Ointment slabs,

f. Mortars (for powder drugs) and pestles,

g. Balances (those of which sensibility reciprocal are 10 mg and 100 mg),

h. Beakers,

i. Sieving equipment,

j. Spatulas (those which are made of metal, horn or equivalent materials),

k. Measuring pipettes and pipette stands,

l. Measuring flasks and measuring cylinders,

m. Spoons (those which are made of metal, horn or equivalent materials),

n. Funnels and funnel stands, and

o. Publications necessary for the dispensing.

(9) To be ensured that the pharmacy to be subjected to the authorisation specified in Item (2) of Article 10 of Enforcement Order of Pharmaceutical Affairs Law (Cabinet Order No.11, 1961) is provided with the following facilities and equipment necessary for the testing, with the proviso that this provision shall not apply to the testing workbenches in case where the dispensing workbenches are used as the testing workbenches and such conduct is verified to present no hindrance to both the testing and dispensing, and to the facilities and equipment specified in **d**., **e**., **g**. and **i**. in case where the testing is conducted on the pharmacy's own responsibilities using the testing institutions specified in Paragraph 1 of Article 12 of Enforcement Regulations of Pharmaceutical Affairs Law (MHW Ordinance No.1, 1961, and hereinafter referred to as "Enforcement Regulations") and such conduct is verified to present no hindrance and to be unavoidable.

a. Microscopes, magnifying lens or X-ray diffractometers for powders,

b. Testing workbenches,

c. Desiccators,

d. Balances (those of which sensibility reciprocal is 1 mg),

e. Thin-layer chromatography apparatuses,

f. Gravimeters or oscillation-type density meters,

g. pH meters,

h. Bunsen burners or alcohol lamps,

i. Disintegration testing apparatuses,

j. Melting point measuring apparatuses, and

k. Publications necessary for the testing.

2. The pharmacy treating the radiopharmaceuticals (the radiopharmaceuticals specified in Item (1) of Article 1 of Radiopharmaceuticals Manufacturing and Handling Regulations (MHW Ordinance No. 4, 1961), and hereinafter referred to as such) shall be provided with the storage rooms which meet the following requirements in addition to those specified in preceding Paragraph 1, with the proviso that this provision shall not apply in case where he/she treats the radiopharmaceuticals in an amount of less than those specified by the Minister of Health, Labour and Welfare.

(1) To be placed where there is little possibility of landslides and flooding,

(2) To be ensured that the main building components, etc. (the main building components and the walls and pillars dividing the interior of the buildings specified in Item (5) of Article 2 in the Building Standard Law (Law No. 201, 1950), and hereinafter referred to as such) are the fire-proof buildings (the fire-proof buildings specified in Item (7) of Article 2 of the Building Standard Law, and hereinafter referred to as such), and to be ensured that the openings are provided with the fire-proof doors which correspond to the specified fire-proof facilities specified in Paragraph 1 of Article 112 of Enforcement Order of Building Standard Law (Cabinet Order No. 338, 1950) (hereinafter referred to as "fire-proof doors" in Item (3) of Paragraph 1 of Article 9), with the proviso that this provision shall not apply in case where the radiopharmaceuticals are stored in the fire-proof containers,

(3) To be provided with the radiation shielding walls or other radiation shielding materials so that the following radiation doses are maintained below the radiation dose limits specified by the Minister of Health, Labour and Welfare,
   a. The radiation dose which the personnel could be exposed to in those places where they routinely enter in the storage rooms, and
   b. The radiation dose on the boundaries of the storage rooms.

(4) To be ensured that the number of the entrances which the personnel routinely pass through is limited to one,

(5) To be provided the part of the storage rooms directly leading to the outside such as doors, hatches, etc. with the facilities or equipment including locks,

(6) To be ensured that the labels specified in attached Table are put to, and

(7) To be provided with the facilities or equipment for preventing spread of contamination with the radiopharmaceuticals.

3. The provision of Item (4) of Paragraph 1 of Article 9 shall be applied *mutatis mutandis* as the standards to the disposing facilities of the pharmacy that dispose of the radioactive substances or the objects contaminated with the radioactive substances. In this case, "work rooms, testing rooms" in **d.**(iv) of same Item shall read "dispensing

rooms”.

4. In case where the dose rate on the surface of the containers or wrappers of the radiopharmaceuticals exceeds the dose rate specified by the Minister of Health, Labour and Welfare in the pharmacy treating the radiopharmaceuticals only in sealed conditions, the dispensing rooms that meet the following requirements shall be provided.

(1) To comply with the provisions of Items (1), (2), (4), (5) and (7) of Paragraph 2, and

(2) To be provided with the radiation shielding walls or other radiation shielding materials that meet the standards specified in Item (3) of Paragraph 2.

5. The provision of Article 9 (excluding Items (3) and (4) of Paragraph 1) shall be applied *mutatis mutandis* as the standards to the buildings and facilities of the pharmacy handling the radiopharmaceuticals in unsealed conditions. In this case, “Articles 6 and 7” in Paragraph1 of same Article shall read “Paragraphs 1, 2 and 3 of Article 1”, “work areas for the products concerned with the radiopharmaceuticals” in Item (2) of same Paragraph shall read “sites for handling the radioactive substances in the pharmacy handling the radiopharmaceuticals” and “work rooms and testing rooms” in **e.** of same Item shall read “dispensing rooms”.

(Buildings and Facilities of Stores of First-Class Distributors)

Article 2 The buildings and facilities of the store of the first-class distributor (excluding the first-class wholesale distributor, and hereinafter referred to as such) shall meet the following requirements.

(1) To be well ventilated and clean,

(2) To be distinctly segregated from the living quarters and unsanitary areas,

(3) To be ensured that the area is at least 13.2 square meters and to allow the appropriate operations of the first-class distributor,

(4) To be provided with the lighting of at least 60 luxes in the areas where the drugs are routinely displayed or delivered,

(5) To be provided with the facilities for storing in a cooled and/or dark condition, with the proviso that this provision shall not apply to the facilities for storing in case where the drugs necessary for being stored in a cooled and/or dark condition are not treated, and

(6) To be provided with the storage facilities that can be locked with locks.

2. The provisions of Paragraphs 2, 3 and 4 of preceding Article shall be applied *mutatis mutandis* to the stores of the first-class distributor treating the radiopharmaceuticals. In this case, "dispensing rooms" in Paragraphs 3 and 4 of same Article shall read "work rooms”.

(Buildings and Facilities of Stores of First-Class Wholesale Distributors)

Article 2-2 The buildings and facilities of the store of the first-class wholesale distributor, which the provisions of Items (1), (2) and (4) to (6) of Paragraph 1 of preceding Article shall be applied *mutatis mutandis* to, shall be provided with the facilities for storing the drugs sanitarily and safely, and the area of the facilities is at least 100 square meters, with the proviso that this provision shall not apply in case where it is verified to present no hindrance to storing the drugs sanitarily and safely and to be unavoidable.

2. The provision of Paragraph 2 of preceding Article shall be applied *mutatis mutandis* to the stores of the first-class wholesale distributor treating the radiopharmaceuticals.

(Buildings and Facilities of Stores of Second-Class Distributors)

Article 3 The buildings and facilities of the store of second-class distributor shall meet the following requirements.

(1) To be well ventilated and clean,

(2) To be distinctly segregated from the living quarters and unsanitary areas,

(3) To be ensured that the area is at least 13.2 square meters and to allow the appropriate operations of the second-class distributor,

(4) To be provided with the lighting of at least 60 luxes in the areas where the drugs are routinely displayed or delivered,

(5) To be provided with the facilities for storing in a cooled and/or dark condition, with the proviso that this provision shall not apply in case where the drugs necessary for being stored in a cooled and/or dark condition are not treated, and

(6) To be provided with the storage facilities that can be locked with locks.

(Buildings and Facilities of Offices of Medical Device Distributors and Leasers)

Article 4 The buildings and facilities of the office of the distributor and leaser of the specially controlled medical devices or the specially designated maintenance-control-required medical devices specified in Paragraph 1 of Article 39 and of the distributor and leaser of the controlled medical devices specified in Paragraph 1 of Article 39-3 of the Pharmaceutical Affairs Law (Law No. 145, 1960) (hereinafter referred to as “Law”) shall meet the following requirements.

(1) To be appropriately lighted, illuminated and ventilated, and clean,

(2) To be distinctly segregated from the living quarters and unsanitary areas, and

(3) To be provided with the facilities necessary for storing the medical devices to handle sanitarily and safely.

(Buildings and Facilities of Offices of Medical Device Repairers)

Article 5 The buildings and facilities of the office of the medical device repairer shall meet the following requirements.

(1) To be provided with the facilities necessary for storing the constituent parts, etc. and the repaired medical devices sanitarily and safely,

(2) To be provided with the facilities and equipment necessary for testing the constituent parts, etc. and the repaired medical devices according to the type of medical devices to repair, with the proviso that this provision shall not apply in case where the testing is conducted on the repairer's own responsibilities using his/her other testing facilities or other testing institutions and such conduct is verified to present no hindrance to the proper testing,

(3) To be provided with the facilities and equipment necessary for conducting the repairing,

(4) To be ensured that the areas for the repairing operations meet the following requirements,

a. Being appropriately lighted, illuminated and ventilated, and clean,

b. Being distinctly segregated from the living quarters and unsanitary areas,

c. Being provided with sufficient area necessary for conducting the operations without hindrance,

d. Being provided with the facilities for controlling dust, humidity, insects and rodents, with the proviso that this provision shall not apply in case where it is verified to present no hindrance according to the medical devices to repair,

e. Being ensured that the floors are made of boards, concrete or materials equivalent thereto, with the proviso that this provision shall not apply in case where it is unavoidable according to the medical devices to repair and the property of the repairing operations, and

f. Being provided with the facilities or equipment necessary for disposing of the waste water and waste materials.

(5) To be ensured that the workbenches in the work rooms present no hindrance to conducting the operations efficiently and appropriately.

Chapter 2 Manufacturers of Drugs, etc.

Section 1 Manufacturers of Drugs

(Buildings and Facilities of Manufacturing Sites of General-Process-Category Drug Manufacturers, etc.)

Article 6 The buildings and facilities of the manufacturing site of the manufacturer in the categories specified in Item (4) of Paragraph 1 and Item (2) of Paragraph 2 of Article 26 and the foreign manufacturers (the foreign manufacturers which are specified in Paragraph 1 of Article 13-3, and referred to as such) in the categories specified in Item (4) of Paragraph 1 and Item (2) of Paragraph 2 of Article 36 of Enforcement Regulations (hereinafter collectively referred to as “manufacturers, etc.”) shall meet the following requirements.

(1) To be provided with the facilities and equipment necessary for manufacturing the products (including those that have undergone the intermediate process and need to undergo subsequent process to be the (final) products (hereinafter referred to as "intermediate products"), and hereinafter referred to as such) in the manufacturing site,

(2) To be placed for preventing the products and raw materials (hereinafter referred to as “products, etc.” from this Article to Article 10) from being mixed up or contaminated and for allowing the efficient and appropriate conduct of the operations without hindrance, and to be those that can be easily cleaned and maintained,

(3) To be provided with the hand-washing facilities, toilets and gowning areas,

(4) To be ensured that the areas where the manufacturing operations are conducted (hereinafter referred to as “work areas”) meet the following requirements,

a. Being appropriately illuminated and ventilated, and clean,

b. Being distinctly segregated from the living quarters and unsanitary areas,

c. Being provided with sufficient area necessary for conducting the operations without hindrance,

d. Being provided with the buildings or facilities for controlling dust, insects and rodents, with the proviso that this provision shall not apply to the work areas where the process prior to the final purification of the products concerned with the active pharmaceutical ingredients provided for the purpose of being used for the manufacturing of drugs (hereinafter referred to as “APIs”) and the manufacturing facilities for such process are the well-closed structure,

e. Being provided with the facilities or equipment necessary for disposing of the waste water and waste materials, and

f. Being provided with the facilities necessary for disposing of the poisonous gases in case where they are handled according to the products, etc. (excluding those concerned with the drugs specified in Cabinet Orders that are provided to be established under the provision of Item (4) of Paragraph 2 of Article 14 of Law).

(5) To be ensured that the work rooms among the work areas for the products concerned with APIs, where the filling operations to the sealing operations in the containers for the intermediate products which have undergone the final purification are conducted, and the work rooms among the work areas for the products other than those concerned with APIs where the weighing operations for the raw materials and the formulating, filling and sealing operations for the products are conducted meet the following requirements,

a. Not being provided with the entrances directly leading to the outside (except those for emergency), with the proviso that this provision shall not apply in case where the work rooms are provided with the buildings and facilities necessary for preventing contamination due to the outside,

b. Being provided with the entrances and windows that can be closed,

c. Being provided the effluent facilities in the work rooms with the structure necessary for preventing contamination of the work rooms,

d. Being provided the ceilings of the work rooms with the structure which does not allow dust to fall, and

e. Being provided the pipes, ducts and other relevant facilities in the work rooms with the structure which does not allow dust to accumulate on their surfaces, with the proviso that this provision shall not apply in case where such facilities can be easily cleaned.

(6) To be provided with the facilities necessary for segregating and storing the products, etc. and packaging and labelling materials sanitarily and safely, and

(7) To be provided with the facilities and equipment necessary for testing the products, etc. and packaging and labelling materials, with the proviso that this provision shall not apply in case where the testing is conducted on the manufacturer's etc. own responsibilities using their other testing facilities or other testing institutions and such conduct is verified to present no hindrance to the proper testing.

(Buildings and Facilities of Manufacturing Sites of Aseptic-Process-Category Drug Manufacturers, etc.)

Article 7 The buildings and facilities of the manufacturing site of the manufacturer, etc. in the categories specified in Item (3) of Paragraph 1 of Article 26 and Item (3) of Paragraph 1 of Article 36 of Enforcement Regulations shall meet the following requirements in addition to those specified in preceding Article.

(1) To be ensured that the work areas meet the following requirements,

a. Being ensured that the work rooms or controlled work areas (the areas consisting of the work rooms, corridors, etc. that are controlled so as to maintain a uniform quality of cleanliness, and hereinafter referred to as such), among the work areas, are provided with the buildings and facilities

for maintaining and controlling the temperature and humidity, and

b. Being ensured that the work rooms for the weighing operations (excluding the operations in the work areas for the products concerned with the aseptic APIs (the aseptic active pharmaceutical ingredients, and hereinafter referred to as such) for the raw materials and the work rooms for the cleaning operations for the containers (in the work areas for the products concerned with aseptic APIs, limited to the containers used in the operations subsequent to the formulating operations for the sterilisation） are the well-closed structure for preventing contamination with dust,

(2) To be ensured that the work rooms for the operations subsequent to the formulating operations for the sterilisation (excluding the case where microbiological growth can be inhibited under the formulation conditions) among the work areas for the products concerned with aseptic APIs, and the work rooms or controlled work areas for the formulating, filling or sealing operations for the drug substances among the work areas for the products concerned with the aseptic drugs (except aseptic APIs) meet the following requirements, and

a. Being provided the ceilings, walls and floors of the work rooms with the surfaces made of materials which are proof against spray cleaning with disinfectant solutions, etc., and

b. Being ensured that the facilities and equipment can be sterilised or disinfected.

(3) To be provided with the following facilities and equipment for the testing. In this case, the proviso of the provision of Item (7) of preceding Article shall be applied *mutatis mutandis*.

a. The facilities and equipment for the hermetic condition tests in case where they are necessary,

b. The facilities and equipment for the testing of foreign particulate matter,

c. The facilities and equipment for the physicochemical testing of the products, etc. and packaging and labelling materials,

d. The facilities and equipment for the sterility tests,

e. The facilities and equipment for the pyrogen tests in case where they are necessary, and

f. The facilities and equipment for the biological tests in case where they are necessary.

(Buildings and Facilities of Manufacturing Sites of Specified Biological-origin Drug Manufacturers, etc.)

Article 8 The buildings and facilities of the manufacturing site of the manufacturer,

etc. of the products concerned with the drugs which correspond to the specified biological-origin products specified in Paragraph 10 of Article 2 of Law, the biological preparations specified in Item (3) **a.** of Paragraph 2 of Article 80 of Enforcement Order of Pharmaceutical Affairs Law (Cabinet Order No. 11, 1961) (excluding the blood preparations which do not constitute a lot and the drugs used exclusively for the diagnosis of disease which do not come into direct contact with the human body), the drugs designated by the Minister of Health, Labour and Welfare in accordance with the provision of Paragraph 1 of Article 43 of Law, the drugs manufactured by application of gene recombination technology, the drugs manufactured using as the raw materials the drugs manufactured by application of gene recombination technology, the drugs manufactured by application of incubation technology of human or animal cells, the drugs manufactured using as the raw materials the drugs manufactured by application of incubation technology of human or animal cells or the cell/tissue-based drugs (hereinafter collectively referred to as "specified biological-origin drugs, etc.") shall meet the following requirements, in addition to those specified in Article 6 (preceding two Articles, in case where the products concerned with sterile drugs are manufactured).

(1) To be ensured that the manufacturing site (excluding the case where the packaging, labelling or storing operations are exclusively conducted) of the products concerned with the specified biological-origin drugs, etc. meet the following requirements, and

a. Being ensured that the clean areas (the places, among the work areas, where the weighing operations for the raw materials or the formulating operations for the drug substances are conducted or where the cleaned containers are exposed to the air in the work areas, and referred to as such in this Item (1)) and the aseptic areas (the places, among the work areas, where the aseptic drug substances or sterilised containers are exposed to the air in the work areas, where the filling operations for the drug substances are conducted, where the sealing operations for the containers are conducted or where the aseptic operations including sterility tests are conducted, and referred to as such in this Item (1)) meet the following requirements,

(i) Being provided the ceilings, walls and floors with smooth surfaces and free from crevices which do not produce dust, and which can be easily cleaned and allow disinfection, and

(ii) Being ensured that the effluent facilities are the appropriate structure for preventing contamination with the poisonous waste waster.

b. Being ensured that the clean areas are not provided with effluent outlets, with the proviso that this provision shall not apply in case where the requirements in the following (i) to (iii) are met and it is verified to be unavoidable,

(i) Being ensured that the effluent outlets are provided with the effluent traps that can be easily cleaned, and the apparatuses for preventing the effluents from flowing backward,

(ii) Being ensured that the effluent traps are the structure that can be disinfected, and

(iii) Being ensured that the grooves of the floors are sufficiently shallow, to be easily cleaned and connected through the effluent outlets to the outside of the manufacturing areas (the places where the incubating,

extracting and purifying operations, the weighing operations for the raw materials, the cleaning and drying operations for the containers, the formulating and filling operations for the drug substances, and the sealing operations for the containers and the packaging operations are conducted as well as the gowning areas, and hereinafter referred to as such in this Item (1)),

c. Being ensured that the aseptic areas meet the following requirements,
- **(i)** Not being provided with the effluent outlets, and
- **(ii)** Not being provided with the washbasins.

d. Being ensured that the areas, among the work areas, for conducting the testing using the animals or microorganisms and those for handling the animal tissue or microorganisms that are not necessary in the manufacturing of the products concerned with the specified biological-origin drugs etc. are distinctly segregated from the areas for manufacturing such products, and the air-handling system is separated from those used for other products,

e. Being ensured that the areas, among the work areas, for conducting the aseptic operations are provided with the buildings and facilities necessary for providing with the clean air treated with the filters and those for controlling appropriately the pressure differential,

f. Being ensured that the areas, among the work areas, where the pathogenic microorganisms are handled are provided with the buildings and facilities necessary for conducting appropriate negative pressure control,

g. Being ensured that the areas, among the work areas, where the infectious microorganisms are handled are provided with the facilities for cleaning, disinfecting and sterilising the equipment used in the areas as well as those for treating the waste liquids,

h. Being ensured that the rooms and the equipment and instruments, among the work areas, used for handling small pox viruses, acute poliomyelitis viruses, spore-forming pathogens or tubercle bacillus mycobacteria for use in the manufacturing are exclusively used for the products according to their type,

i. Being ensured that the air-handling system meets the following requirements,
- **(i)** Being the proper structure for preventing the products, etc. from being contaminated with microorganisms, etc.,
- **(ii)** In case where pathogenic microorganisms, etc. are handled, being appropriate structure for preventing such microorganisms, etc. from spreading into the air,
- **(iii)** Being the structure which discharges the air exhausted from the areas for handling the pathogenic microorganisms, etc. after removal of such microorganisms, etc. with the high-efficiency particulate air (HEPA) filter,
- **(iv)** Being the structure which does not recirculate the air exhausted from the work rooms that could leak the pathogenic microorganisms, etc.,

with the proviso that this provision shall not apply in case where such microorganisms etc. are sufficiently removed by the structure specified in preceding (iii) and it is verified that such recirculation is unavoidable, and

(v) Being ensured that the air-handling system is separated from those used for other work rooms, where necessary.

j. Being ensured that the pipes, valves and vent filters are the structure that can be easily cleaned and sterilised according to the purpose of the use,

k. Being ensured that the premises for controlling the animals utilised in the manufacturing or testing (including the donor animals, hereinafter referred to as "utilised animals") meet the following requirements, and

(i) Being ensured that the quarantine areas for the utilised animals are segregated from other areas,

(ii) Being ensured that the storage facilities for the feed could not be infested by insects,

(iii) Being provided with the keeping rooms for the animals utilised in the manufacturing as well as those for the animals utilised in the testing separately,

(iv) Being ensured that the air-handling system used for the keeping rooms for the utilised animals is separated from those for other areas, with the proviso that this provision shall not apply to the utilised animals which are verified proper to be kept outside, and

(v) Being provided with the rooms for inoculating the antigens, etc. into the utilised animals in case where they conduct such inoculation. In this case, the rooms for the inoculation shall be segregated from the autopsy rooms.

l. Providing the storage facilities with the constant temperature apparatuses, self-recording thermometers and other necessary measuring equipment.

(2) To be ensured that the buildings and facilities of the manufacturing site (excluding those which conduct exclusively packaging, labelling or storing) for the products concerned with the cell/tissue-based drugs (drugs composed of human or animal cells or tissue (excluding human blood and the drugs which compose of the components manufactured using human blood), and hereinafter referred to as such) meet the following requirements in addition to those specified in preceding Item (1).

a. Being ensured that the areas for receiving and processing the raw materials, storing the products, etc. are segregated from other areas for manufacturing the products, and

b. Being provided the areas for receiving and processing the raw materials, storing the products, etc. with the buildings and facilities necessary for conducting such operations.

2. The manufacturing sites (limited to those which conduct exclusively packaging, labelling or storing) of the products concerned with the specified biological-origin drugs, etc. shall be provided with sufficient area for conducting appropriately the operations

without hindrance.

(Buildings and Facilities of Manufacturing Sites of Radiopharmaceuticals-Category Drug Manufacturers, etc.)

Article 9 The buildings and facilities of the manufacturing site (excluding those where the packaging, labelling or storing operations are exclusively conducted, and hereinafter referred to as such in this Article and next Article) of the manufacturer, etc. in the categories specified in Item (2) of Paragraph 1 and Item (1) of Paragraph 2 of Article 26 and Item (2) of Paragraph 1 and Item (1) of Paragraph 2 of Article 36 of Enforcement Regulations shall meet the following requirements in addition to those specified in preceding Articles 6 and 7.

(1) To be placed where there is little possibility of landslides and flooding,

(2) To be ensured that the work areas for the products concerned with the radiopharmaceuticals meet the following requirements,

a. Being distinctly segregated from other premises,

b. Being ensured that the main building components, etc. are the fire-proof buildings or are made of the noninflammable materials (the noninflammable materials specified in Item (9) of Article 2 of Building Standard Law, and hereinafter referred to as such),

c. Being provided with the radiation shielding walls or other shielding materials so as the following radiation doses are maintained below the radiations dose limits specified by the Minister of Health, Labour and Welfare,

(i) The radiation dose which the personnel could be exposed to in those places where they routinely enter in the storage rooms, and

(ii) The radiation dose on the boundaries of the manufacturing site and in the living quarters in the manufacturing site.

d. Being ensured that the number of the entrances which the personnel routinely pass through is limited to one,

e. Being provided with the work rooms and the testing rooms (including the animal test rooms in case where the animal tests are conducted, and hereinafter referred to as such), and

(i) Being ensured that the walls, floors and other parts of the interior of the rooms which could be contaminated with the radioactive substances (the radioactive substances specified in Item (2) of Article 1 of Radiopharmaceuticals Manufacturing and Handling Regulations, and hereinafter referred to as such) are the buildings finished to have minimal protrusions, hollows or crevices such as joints of the finishing materials,

(ii) Being ensured that the surfaces of the walls, floors or other parts of the interior of the rooms which could be contaminated with the radioactive substances are smooth and finished with the materials

which are resistant to infiltration of gases or liquids and to corrosion,

(iii) Being provided with the disposal containers that could not allow the disposed radioactive substances or the disposed objects contaminated with the radioactive substances to disperse, leak, soak through nor flow out and allow the safe transportation and disposal, and

(iv) Being provided with the hoods, glove boxes and other apparatuses for preventing spread of the gaseous radioactive substances or the air contaminated with the radioactive substances in connection with the exhaust facilities.

f. Being provided with the contamination testing rooms (the rooms for conducting the testing and removal of the contamination with the radioactive substances on the surfaces of the human bodies or the items worn thereon such as clothes, work shoes and protective items, and hereinafter referred to as such), with the proviso that this provision shall not apply in case where the radioactive substances are handled in an amount of less than those specified by the Minister of Health, Labour and Welfare.

(i) Being placed where is the most proper for conducting the testing and removal of the contamination with the radioactive substances, such as the entrances of the work areas where the personnel routinely enter,

(ii) Meeting the requirements specified in preceding **e.** (i) and (ii),

(iii) Being provided with the cleaning facilities and gowning facilities as well as the radiation meters for conducting the testing of the contamination and the equipment and materials necessary for removing the contamination, and

(iv) Being ensured that the effluent pipes for the cleaning facilities specified in preceding (iii) are connected to the effluent facilities.

(3) To be provided with the storage facilities that meet the following requirements,

a. Being provided with the storage rooms of which main building components, etc. are the fire-proof buildings and of which openings are provided with the fire-proof doors, or with the storage boxes which are the fire-proof buildings,

b. Being provided with the radiation shielding walls or other shielding materials that meet the requirements specified in preceding Item (2) **c.,**

c. Being ensured that the number of the entrances which the personnel routinely pass through is limited to one,

d. Being provided the part of the storage facilities directly leading to the outside such as doors, hatches, etc. with the facilities or equipment including locks,

e. Being provided with the facilities or equipment that can be locked with locks for storing the radiopharmaceuticals segregated from other objects,

f. Being provided with the containers of the radioactive substances, which meet the following requirements,

(i) Being ensured that the containers of the radioactive substances which could contaminate the air out of the containers are the airtight structure,

(ii) Being ensured that the containers of the liquid radioactive substances are the structure resistant to the spilling, and are made of the materials resistant to the infiltration of them, and

(iii) Being ensured that the containers of liquid or solid radioactive substances, in case where they could have accidents such as being cracked and broken, are provided with the facilities or equipment for preventing spread of the contamination with the radioactive substances, such as the receiving trays and absorbent materials.

(4) To be provided with the disposal facilities which meet the following requirements,

a. Being distinctly segregated from other premises,

b. Being ensured that the main building components, etc. are the fire-proof buildings or are made of the noninflammable materials,

c. Being provided with the radiation shielding walls or other shielding materials that meet the requirements specified in preceding Item (2) **c.,**

d. Being provided with the exhaust facilities which meet the following requirements, with the proviso that this provision shall not apply in case where they handle the radioactive substances in an amount of less than those specified by the Minister of Health, Labour and Welfare and where the gaseous radioactive substances are not produced nor the air could not be contaminated with the radioactive substances,

(i) Being provided with the capacity to maintain the concentration of the radioactive substances in the exhaust air at the exhaust port, or to maintain the concentration of the radioactive substances in the air outside the boundaries of the manufacturing site by monitoring the concentration with the exhaust monitoring facilities (in case where they have taken measures to prevent access of the personnel to the areas adjacent to the boundaries of the manufacturing site, the boundaries of the areas, and hereinafter referred to as such in this Item (4)) below the concentration limit specified by the Minister of Health, Labour and Welfare,

(ii) Being the structure resistant to leakage of gases, and being made of the materials resistant to corrosion,

(iii) Being provided with the apparatuses for preventing rapidly the spread of the air contaminated by the radioactive substances in the event of the failure of the exhaust facilities, and

(iv) Being provided with the capacity to maintain the concentration of the radioactive substances in the air in the areas where the personnel routinely enter in the work rooms, testing rooms or disposing work rooms (the rooms where the operations for incinerating the radioactive substances or objects contaminated with the radioactive substances and removing their residues from the incinerators, or the operations for solidifying (including the treatment for the solidification, and

hereinafter referred as such) the radioactive substances or objects contaminated with the radioactive substances with concrete or other solidifying materials are conducted, and hereinafter referred to as such) below the concentration limit specified by the Minister of Health, Labour and Welfare.

e. Being provided with the effluent facilities which meet the following requirements, in case where they decontaminate or drain the liquid radioactive substances or the liquid contaminated with the radioactive substances,

(i) Being provided with the capacity to maintain the concentration of the radioactive substances in the effluent liquids at the effluent outlets, or to maintain the concentration of the radioactive substances in the effluents at the boundaries of the manufacturing site by monitoring the concentration with the effluent monitoring facilities below the concentration limit designated by the Minister of Health, Labour and Welfare,

(ii) Being the structure resistant to leakage of effluents and being made of the materials resistant to infiltration of the effluents and to corrosion,

(iii) Being ensured that the effluent purification tanks are the structure which allows to sample the effluents or to measure the concentration of the radioactive substances in the effluents, and are provided with the apparatuses for adjusting the flow rate of the effluents, and

(iv) Being ensured that the openings on top of the effluent purification tanks are the structure which can be covered, or are provided with the fences or other facilities for preventing the access of the personnel.

f. The provisions of preceding **d.**(i) or **e.**(i) shall not apply, in case where it is extremely difficult to be provided with the exhaust facilities or the effluent facilities which have the capacity specified in **d.**(i) or **e.**(i), and the Minister of Health, Labour and Welfare has approved that such facilities are provided with the capacity to maintain the radiation dose which the personnel outside the boundaries of the manufacturing site are exposed to below the radiation dose limit specified by the Minister of Health, Labour and Welfare,

g. In case where it is deemed that the exhaust facilities or the effluent facilities which has been approved as specified in preceding **f.** does not to have the capacities concerned with such approvals, the Minister of Health, Labour and Welfare may cancel such approvals,

h. In case where the radioactive substances or the objects contaminated with the radioactive substances are incinerated, to be provided with the exhaust facilities meeting the requirements specified in preceding **e.**, the disposing work rooms meeting the requirements specified in **e. (i)**, **(ii)** and **(iv)** of preceding Item (2), the contamination testing rooms meeting the requirements specified in **f. (i)** to **(iii)** of same Item, and the incinerators meeting the following requirements,

(i) Being the buildings resistant to leakage of the gases and dispersion of the ash,

(ii) Being connected with the exhaust facilities, and

(iii) Being ensured that the outlets for the incineration residues are connected with the disposing work rooms.

i. In case where the radioactive substances or the objects contaminated with the radioactive substances are solidified with concrete or other solidifying materials, to be provided with the exhaust facilities meeting the requirements specified in preceding **e.**, the disposing work rooms meeting the requirements specified in **e.(i)**, **(ii)** and **(iv) of** preceding Item (2), the contamination testing rooms meeting the requirements specified in **f. (i)** to **(iii)** of same Item, and the solidification facilities meeting the following requirements, and

(i) Being the structure resistant to leakage or spilling of the radioactive substances or the objects contaminated with the radioactive substances and dispersion of the powder dust, and

(ii) Being made of the materials resistant to the infiltration of the liquids and to corrosion.

j. In case where the radioactive substances or the objects contaminated with the radioactive substances are stored and/or disposed of, to be provided with the storing and disposing facilities meeting the following requirements.

(i) Being the structure segregated from the outside,

(ii) Being ensured that the doors, hatches and other parts of the storing and disposing facilities leading to the outside are provided with locks or other facilities or equipment for closing, and

(iii) Being provided with the containers (limited to those which are provided with the fire-proof structure) meeting the requirements specified in **f**. of preceding Item (3).

(5) To be ensured that the boundaries of the controlled areas specified in Item (3) of Article 1 of Radiopharmaceuticals Manufacturing and Handling Regulations are provided with the fences or other facilities for preventing the access of the personnel.

2. The provisions of Items (1), (2) **b.** to **e.**, (3) **a.** to **d.** and **f.**, (4) and (5) of preceding Paragraph 1 shall not apply in case where only the radioactive substances in an amount of less than those specified by the Minister of Health, Labour and Welfare are handled.

3. The provisions of preceding two Paragraphs 1 and 2 (excluding: the provisions concerned with the work rooms specified in Item (2) **e**. and Item (4) **d**. of preceding Paragraph 1, in case where the packaging, labelling or storing of the objects concerned with the containers or wrappers specified in the proviso of the provision of Item (1) of Paragraph 3 of Article 2 of Radiopharmaceuticals Manufacturing and Handling Regulations of is exclusively conducted; and the provisions concerned with the testing rooms specified in Item (2) **e.** and Item (4) **d.** of preceding Paragraph 1, in case where the testing is conducted on the manufacturer's, etc. own responsibilities using their other testing facilities or other testing institutions and such conduct is verified to present no hindrance to the proper testing) shall be applied *mutatis mutandis* to the buildings and facilities of the manufacturing site of the manufacturers, etc. (limited to those which exclusively conduct packaging, labelling or storing) in the categories specified in Item (2) of Paragraph 1 and Item (1) of Paragraph 2 of Article 26 and Item (2) of Paragraph 1

and Item (1) of Paragraph 2 of Article 36 of Enforcement Regulations.

(Buildings and Facilities of Manufacturing Sites for Packaging, etc.-Process-Category Drug Manufacturers, etc.)

Article 10 The buildings and facilities of manufacturing site of the manufacturer in the categories specified in Item (5) of Paragraph 1 and Item (3) of Paragraph 2 of Article 26 and Item (5) of Paragraph 1 and Item (3) of Paragraph 2 of Article 36 of Enforcement Regulations shall meet the following requirements.

(1) To be provided with the buildings and facilities necessary for storing the products, etc. and packaging and labelling materials sanitarily and safely,

(2) To be provided with sufficient area for conducting appropriately the operations without hindrance, and

(3) To be provided with the facilities and equipment necessary for testing the products, etc. and packaging and labelling materials, with the proviso that this provision shall not apply in case where the testing is conducted on the manufacturer's etc. own responsibilities using their other testing facilities or other testing institutions and such conduct is verified to present no hindrance to the proper testing.

(Exceptions in Manufacturing of Drugs in Pharmacies)

Article 11 The requirements specified in Paragraph 1 of Article 1 shall, notwithstanding the provision of Article 6, be applied to the buildings and facilities of the manufacturing site in the pharmacy, in case where the drugs (excluding injectable drugs) which can be manufactured under the simple and physical operations such as mixing and dissolving and which can be manufactured using the buildings and facilities and the equipment of the pharmacy specified in Paragraph 1 of Article 1 are manufactured in so far as the pharmacy manager can conduct complete control of such manufacturing to the extent which is verified to present no hindrance to the conduct of the operations in the pharmacy.

Section 2 Quasi-drug manufacturers

(Buildings and Facilities of Manufacturing Sites for General-Process-Category Quasi-drug Manufacturers, etc.)

Article 12 The buildings and facilities of the manufacturing site of the manufacturer, etc. in the categories specified in Item (2) of Paragraph 3 of Article 26 and Item (2) of Paragraph 3 of Article 36 of Enforcement Regulations shall meet the following requirements, with the proviso that the provision of Article 6 shall be applied *mutatis mutandis* to the quasi-drugs specified in Cabinet Ordinances that are provided to be established under the provision of Item (4) of Paragraph 2 of Article 14 of Law.

(1) To be provided with the facilities and equipment necessary for manufacturing the products of the manufacturing site,

(2) To be ensured that the work areas meet the following requirements,

a. Being appropriately illuminated and ventilated, and clean,

b. Being distinctly segregated from the living quarters and unsanitary areas,

c. Being provided with sufficient area necessary for conducting the operations without hindrance,

d. Being provided with the facilities for controlling dust, insects and rodents,

e. Being ensured that the floors are made of boards, concrete or materials equivalent thereto,

f. Being provided with the facilities or equipment for disposing of the waste water and waste materials,

g. Being provided with the facilities for disinfecting the personnel, and

h. Being provided with the facilities necessary for disposing of the poisonous gases in case where they are exhausted according to the quasi-drugs.

(3) To be ensured that the work rooms, among the work areas, where the weighing operations for the raw materials or the formulating, filling or sealing operations for the quasi-drugs are conducted meet the following requirements,

a. Being ensured that the workbenches in work rooms present no hindrance to conducting the operations efficiently and appropriately,

b. Being ensured that the work rooms are the buildings which do not to allow passage of the personnel other than those conducting operations in such work rooms, with the proviso that this provision shall not apply in case where the quasi-drugs could not be contaminated by the personnel other than those conducting operations in such work rooms,

c. Being provided with the entrances and windows that can be closed,

d. Being ensured that the ceilings are made of boards, concrete or materials equivalent thereto and are finished so as not to allow dust to fall,

e. Being provided the floors with smooth and gap-free surfaces made of concrete, tiles, mortar, boards or other materials which allow removal of stains to the extent equivalent thereto, and

f. Being provided the pipes, ducts and other relevant facilities in the work rooms with the structure which does not allow dust to accumulate on their surfaces, with the proviso that this provision shall not apply in case where such facilities can be easily cleaned.

(4) To be provided with the facilities for storing the raw materials, packaging and labelling materials and products sanitarily and safely, and

(5) To be provided with the facilities and equipment necessary for testing the products, etc. and packaging and labelling materials, with the proviso that this provision shall not apply in case where the testing is conducted on the manufacturer's, etc. own responsibilities using their other testing facilities or other testing institutions and such conduct is verified to present no hindrance to the proper testing.

(Buildings and Facilities of Manufacturing Sites of Aseptic-Process-Category Quasi-drug Manufacturers, etc.)

Article 12-2 The provisions of preceding Article and Article 7 (excluding those provided in Article 6) shall be applied *mutatis mutandis* to the buildings and facilities of the manufacturing site of the manufacturer, etc. in the categories specified in Item (1) of Paragraph 3 of Article 26 and Item (1) of Paragraph 3 of Article 36 of Enforcement Regulations.

(Buildings and Facilities of Manufacturing Sites of Packaging, etc.-Process-Category Quasi-drug Manufacturers, etc.)

Article 12-3 The provision of Article 10 shall be applied *mutatis mutandis* to the buildings and facilities of the manufacturing site of the manufacturer, etc. in the categories specified in Item (3) of Paragraph 3 of Article 26 and Item (3) of Paragraph 3 of Article 36 of Enforcement Regulations.

Section 3 Manufacturers of Cosmetics

(Buildings and Facilities of Manufacturing Sites of General-Process-Category Cosmetics Manufacturers)

Article 13 The buildings and facilities of the manufacturing site of the manufacturers in the category specified in Item (1) of Paragraph 4 of Article 26 of Enforcement Regulations shall meet the following requirements.

(1) To be provided with the facilities and equipment necessary for manufacturing the products of the manufacturing site,

(2) To be ensured that the work areas meet the following requirements,

a. Being appropriately ventilated and clean,

b. Being distinctly segregated from the living quarters and unsanitary areas,

c. Being provided with sufficient area necessary for conducting the operations without hindrance,

d. Being provided with the buildings or facilities for controlling dust, insects and rodents,

e. Being ensured that the floors are made of boards, concrete or materials equivalent thereto,

f. Being provided with the facilities or equipment for disposing of the waste water and waste materials,

(3) To be provided with the facilities for storing the products, raw materials and packaging and labelling materials sanitarily and safely, and

(4) To be provided with the facilities and equipment necessary for testing the products, raw materials and packaging and labelling materials, with the proviso that this provision shall not apply in case where the testing is conducted on the manufacturer's, etc. own responsibilities using their other testing facilities or other testing institutions and such conduct is verified to present no hindrance to the proper testing.

(Buildings and Facilities of Manufacturing Sites of Packaging, etc.-Process-Category Cosmetics Manufacturers)

Article 13-2 The provision of Article 10 shall be applied *mutatis mutandis* to the buildings and facilities of the manufacturing site of the manufacturer in the category specified in Item (2) of Paragraph 4 of Article 26 of Enforcement Regulations. In this case, "manufacturer's, etc." in Item (3) of Article 10 shall read "manufacturer's".

(Buildings and Facilities of Manufacturing Sites of General-Process-Category Medical Device Manufacturers, etc.)

Article 14 The buildings and facilities of the manufacturing site for the manufacturer, etc. in the categories specified in Item (3) of Paragraph 5 of Article 26 and Item (3) of Paragraph 4 of Article 36 of Enforcement Regulations shall meet the following requirements.

(1) To be provided with the facilities and equipment necessary for manufacturing the products of the manufacturing site,

(2) To be placed for allowing the efficient and appropriate conduct of the operations without hindrance, and to be those that can be easily cleaned and maintained,

(3) To be provided with the hand-washing facilities, toilets and gowning areas,

(4) To be ensured that the work areas meet the following requirements,

a. Being appropriately illuminated and ventilated, and clean,

b. Being distinctly segregated from the living quarters and unsanitary areas,

c. Being provided with sufficient area necessary for conducting the operations without hindrance,

d. Being provided with the buildings or facilities for controlling dust, humidity, insects and rodents, with the proviso that this provision shall not apply in case where it is verified to present no hindrance according to the products,

e. Being provided with the facilities or equipment necessary for disposing of the waste water and waste materials, and

f. Being provided with the facilities necessary for disposing of the poisonous gases in case where they are handled according to the products (excluding those concerned with the medical devices specified in Cabinet Orders that are provided to be established under the provision of Item (4) of Paragraph 2 of Article 14 of Law).

(5) To be provided with the facilities for segregating and storing the products, process agents (objects that are used for the intermediate products in the manufacturing processes (excluding those that constitute parts of the product)) and constituent parts, etc. (parts, assemblies (limited to those that are used in the products), raw materials, materials, containers, wrappers, labellings (including package inserts), etc., that are used in the manufacturing processes and constitute parts of the product, as well as software of the product, and hereinafter referred to as such) sanitarily and safely, and

(6) To be provided with the facilities and equipment necessary for testing the products, process agents and constituent parts, etc. (hereinafter referred to as “products, etc.” from this Article to Article 14-4), with the proviso that this provision shall not apply in case where the testing is conducted on the manufacturer's, etc. own responsibilities using their other testing facilities or other testing institutions and such conduct is verified to present no hindrance to the proper testing.

(Buildings and Facilities of Manufacturing Sites of Sterile-Medical-Device-Category Manufacturers, etc.)

Article 14-2 The buildings and facilities of the manufacturing site of the manufacturer, etc. in the categories specified in Item (2) of Paragraph 5 of Article 26 and Item (2) of Paragraph 4 of Article 36 shall meet the following requirements in addition to those specified in preceding Article.

(1) To be ensured that the work rooms or controlled work areas (hereinafter referred to as "controlled work areas, etc.") for conducting the assembling operations and packaging operations for the products concerned with sterile medical devices meet the following requirements,

a. Being ensured that the controlled work areas, etc. are the buildings which do not allow passage of the personnel other than those conducting operations in such controlled work areas, etc., with the proviso that this provision shall not apply in case where the products could not be contaminated by the personnel other than those conducting operations in such controlled work areas, etc.,

b. Not being provided with the entrances directly leading to the outside (except those for emergency), with the proviso that this provision shall not apply in case where the controlled work areas, etc. are provided with the buildings and facilities necessary for preventing contamination due to the outside,

c. Being provided with the entrances and windows that can be closed,

d. Being provided the ceilings, walls and floors of the controlled work areas, etc. with the surfaces made of materials which are proof against spray washing with disinfectant solutions, etc.,

e. Being provided the effluent facilities, in case where they are provided in the controlled work areas, etc., with the buildings necessary for preventing contamination of the controlled work areas, etc., and

f. Being segregated from the work areas for the products other than those concerned with sterile medical devices, with the proviso that this provision shall not apply in case where the products concerned with sterile medical devices could not be contaminated.

(2) To be ensured that the controlled work areas, etc. where the personnel routinely enter are provided with the gowning rooms meeting the following requirements exclusively used for the personnel who conduct operations in such controlled work areas, etc., and

a. Not being provided with the entrances directly leading to the outside (except those for emergency), and

b. Being provided with the structures and facilities for maintaining the appropriate degree of cleanliness.

(3) To be ensured that the work rooms for conducting the sterilisation operations meet the following requirements.

a. Being ensured that such work rooms are the buildings which do not allow passage of the personnel other than those conducting operations in such work rooms, with the proviso that this provision shall not apply in case where the products could not be contaminated by the personnel other than those conducting operations in such work rooms,

b. Being provided with the entrances and windows that can be closed, and

c. Being provided the ceilings, walls and floors with the surfaces which allow easy removal of stains.

(Buildings and Facilities of Manufacturing Sites of Specified Biological-origin Medical Device Manufacturers, etc.)

Article 14-3 The buildings and facilities of the manufacturing site (excluding those which exclusively operate packaging, labelling or storing, and referred to as such in this Paragraph) of the manufacturer, etc. of the products concerned with the medical devices which correspond to the specified biological-origin products specified in Paragraph 10 of Article 2 of Law, the medical devices designated by Minister of Health, Labour and Welfare in accordance with the provision of Paragraph 2 of Article 43 of Law, or the cell/tissue-based medical devices (hereinafter collectively referred to as “specified biological-origin medical devices, etc.”) shall meet the following requirements in addition to those specified in Article 14 (preceding two Articles, in case where the

products concerned with sterile medical devices are manufactured).

(1) To be ensured that the work areas meet the following requirements,

a. Being ensured that the work rooms or controlled work areas for manufacturing the products concerned with the specified biological-origin medical devices etc. are provided with the buildings and facilities for maintaining and controlling the temperature and humidity,

b. Being ensured that the work rooms for the weighing operations for the materials and the work rooms for the cleaning operations for the container are the well-closed structure for preventing contamination with dust,

c. Being ensured that the clean areas (the places, among the work areas, where the weighing operations and formulating operations for the constituent parts, etc. are conducted and where the cleaned containers are exposed to the air in the work areas, and referred to as such in this Item (1)) and the aseptic areas (the places, among the work areas, where the aseptic products, intermediate products or constituent parts, etc. or the sterilised containers are exposed to the air in the work areas, where the sealing operations for the containers are conducted or where the aseptic operations including sterility tests are conducted, and referred to as such in this Item (1)) meet the following requirements,

(i) Being provided with the ceilings, walls and floors with smooth surfaces and free from crevices which do not produce dust, and

(ii) Being ensured that the effluent facilities are the appropriate structure for preventing contamination with the poisonous effluents.

d. Being ensured that the clean areas are not provided with effluent outlets, with the proviso that this provision shall not apply in case where the requirements in the following (i) to (iii) are met and it is verified to be unavoidable,

(i) Being ensured that the effluent outlets are provided with the effluent traps that can be easily cleaned and the apparatuses for preventing the effluents from flowing backward,

(ii) Being ensured that the effluent traps are the structure that can be disinfected, and

(iii) Being ensured that the grooves of the floors are sufficiently shallow, to be easily cleaned and connected through the effluent outlets to the outside of the manufacturing areas (the places where the incubating, extracting and purifying operations, the weighing and formulating operations for the constituent parts, etc., the cleaning and drying operations for the containers, the sealing operations for the containers and the packaging operations are conducted as well as the gowning areas).

e. Being ensured that the aseptic areas meet the following requirements,

(i) Not being provided with the effluent outlets, and

(ii) Not being provided with the washbasins.

f.. Being ensured that the areas for conducting the testing using the animals or microorganisms and those for handling the animal tissue or microorganisms that are not necessary in the manufacturing of the products concerned with the specified biological-origin medical devices etc. are distinctly segregated from the areas for manufacturing such products, and the air-handling system is separated from those used for other products,

g. Being ensured that the areas for conducting the aseptic operations are provided with the buildings and facilities necessary for providing with the clean air treated with the filters and those for controlling appropriately the pressure differential,

h. Being ensured that the areas, among the work areas, where the pathogenic microorganisms are handled are provided with the buildings and facilities necessary for conducting appropriate negative pressure control, and

i. Being ensured that the areas, among the work areas, where the infectious microorganisms are handled are provided with the facilities for cleaning, disinfecting and sterilising the equipment used in the areas as well as those for treating the waste liquids, etc.

(2) To be ensured that the rooms provided with the facilities, among the facilities necessary for conducting the testing of the products, process agents and materials, for conducting the sterility tests meet the following requirements,

a. Being aseptic rooms, with the proviso that this provision shall not apply in case where such work rooms are provided with facilities which have functions to allow that the aseptic operations are conducted without hindrance according to the type, manufacturing procedures, etc. of the products, and

b. Being ensured that, in the aseptic rooms specified in preceding **a.** are provided with the adjourning anterooms exclusively used for the rooms so that the rooms are routinely accessible only through such anterooms, and not being placed the entrances of the anterooms directly leading to the outside.

(3) To be ensured that the work areas are provided with the following facilities,

a. The facilities necessary for keeping the animals utilised in the manufacturing or testing,

b. The facilities for formulating the culture media and their diluted solution,

c. The facilities necessary for cleaning, drying, sterilising and storing the equipment and instruments, containers, etc. for use in the manufacturing or testing,

d. The facilities for sealing the containers, and

e. The facilities for appropriately disposing of the animal carcasses and other wastes as well as for decontaminating the sewage.

(4) To provide the storage facilities with the constant temperature apparatuses, self-recording thermometers and other necessary measuring equipment,

(5) To be ensured that the air-handling system meets the following requirements,

a.. Being appropriate buildings for preventing the products or materials from being contaminated with microorganisms, etc.,

b. In case where pathogenic microorganisms, etc. are handled, being appropriate structure for preventing such microorganisms, etc. from spreading into the air,

c. Being the structure which discharges the air exhausted from the areas for handling the pathogenic microorganisms, etc. after removal of such microorganisms, etc. with the high-efficiency particulate air (HEPA) filter,

d. Being the structure which does not recirculate the air exhausted from the work rooms that could leak the pathogenic microorganisms, etc., with the proviso that this provision shall not apply in case where such microorganisms, etc. are sufficiently removed by the buildings specified in preceding **c.**, and it is verified that such recirculation is unavoidable, and

e. Being ensured that the air-handling system is separated from those used for other work rooms, where necessary.

(6) To be ensured that the pipes, valves and vent filters are the structure that can be easily cleaned and sterilised according to the purpose of the use,

(7) To be provided with the following facilities and equipment for the testing. In this case, the proviso of the provision of Item (6) of Article 14 shall be applied *mutatis mutandis*, and

a. The facilities and equipment for the hermetic condition tests in case where they are necessary,

b. The facilities and equipment for the testing of foreign particulate matter,

c. The facilities and equipment for the physicochemical testing of the products, process agents and materials,

d. The facilities and equipment for the sterility tests,

e. The facilities and equipment for the pyrogen tests in case where they are necessary, and

f. The facilities and equipment for the biological tests in case where they are necessary.

(8) To be ensured that the premises for controlling the animals utilised in the manufacturing or testing (hereinafter referred to as "utilised animals") meet the following requirements.

a. Being ensured that the quarantine areas for the utilised animals are segregated from other areas,

b. Being ensured that the storage facilities for the feed could not be infested by insects,

c. Being provided with the keeping rooms for the animals utilised in the manufacturing as well as those for the animals utilised in the testing separately,

d. Being ensured that the air-handling system used for the keeping rooms for utilised animals is segregated from other areas, with the proviso that this provision shall not apply to the utilised animals which are verified proper to be kept outside, and

e.. Being provided with the rooms for inoculating the antigens, etc. into the utilised animals in case where they conduct such inoculation. In this case, the rooms for the inoculation shall be segregated from the autopsy rooms.

2. The work areas of the manufacturing site (limited to those which conduct exclusively packaging, labelling or storing) of the manufacturers, etc. of the products concerned with the specified biological-origin medical devices, etc. shall be provided with sufficient area for conducting appropriately the operations without hindrance.

(Buildings and Facilities of Manufacturing Sites of Labelling, etc.-Category Medical Device Manufacturers, etc.)

Article 14-4 The buildings and facilities of the manufacturing site of the manufacturer, etc. in the categories specified in Item (4) of Paragraph 5 of Article 26 and Item (4) of Paragraph 4 of Article 36 of Enforcement Regulations shall meet the following requirements.

(1) To be provided with the buildings and facilities necessary for storing the products, etc. sanitarily and safely,

(2) To be provided with sufficient area for conducting appropriately the operations without hindrance, and

(3) To be provided with the facilities and equipment necessary for testing the products, etc., with the proviso that this provision shall not apply in case where the testing is conducted on the manufacturer's, etc. own responsibilities using their other testing facilities or other testing institutions and such conduct is verified to present no hindrance to the proper testing.