

## Tentative translation of MHLW MO 169 revised in 2021, Chapter 5

(Note)

- 1) This English document is only for reference purpose. In case of any discrepancy, the Japanese text shall prevail.
- 2) The requirements of MHLW MO 169 are applied to both the Marketing Authorization Holder and the person operating the Registered Manufacturing Site. In this document the requirements are stipulated as the requirements for the Marketing Authorization Holder. Meanwhile, when they are applied to the Registered Manufacturing Site, the requirements must be paraphrased, as appropriate.

### Chapter 5. Manufacturing control and quality control of radioactive *in vitro* diagnostics

(Infrastructure for operation at a registered manufacturing site of radioactive *in vitro* diagnostics)

Article 80 Marketing authorization holders, etc. of products related to radioactive *in vitro* diagnostics shall meet the following requirements as an infrastructure for operation at a registered manufacturing site (excluding registered manufacturing sites where only design is performed; the same shall apply in this chapter) of the products (for a registered manufacturing site where only packaging, labeling, or storage of containers or wrappers specified in the proviso of Item 1, Paragraph 3, Article 2 of the Regulations for Manufacturing and Handling of Radiopharmaceuticals is conducted, provisions related to work rooms in E of Item 2 and D of Item 4 shall be excluded, and provisions related to testing rooms in E of Item 2 and D of Item 4 are excluded if such testing is conducted on its own responsibility by using other testing facilities of the registered manufacturing site or other testing institutions and if it is found that there is no problem).

[1] It should be installed in a place where there is less risk of a landslide and flood.

[2] Work areas for products related to radioactive *in vitro* diagnostics shall conform to the following requirements.

A. They should be clearly separated from the other facilities.

B. A main structure, etc. is fireproof or made of non-combustible materials (non-combustible materials specified in Item 9, Article 2 of the Building Standards Act [Act No. 201 of 1950]; the same shall apply hereinafter).

C. Shielding walls or other shielding materials necessary to control the following doses at or below the dose limit specified by the Minister of Health, Labour and Welfare are installed.

(1) Radiation dose to which people may be exposed in a place where people in a registered

manufacturing site always enter

(2) Radiation dose at the boundary of a registered manufacturing site and in an area where people in a registered manufacturing site inhabit

D. There shall be only one entrance/exit site, where people enter/leave on a routine basis.

E. There should be work rooms and testing rooms (including animal testing rooms if animal testing is performed; the same shall apply hereinafter) conforming to the following requirements.

(1) Internal walls, floors, and other parts that may be contaminated by radioactive substances (radioactive substances specified in Item 2, Article 1 of the Regulations for Manufacturing and Handling of Radiopharmaceuticals; the same shall apply hereinafter) shall have a structure with few gaps, such as protrusions, dents, and joint of finishing materials.

(2) The surfaces of inner walls, floors, and other parts that may be contaminated by radioactive substances shall be flat and smooth and finished with materials that are difficult to be penetrated and corroded by gases or liquids.

(3) There should be disposal containers that are free from risk of scattering, leaking, seepage, or flow of radioactive substances or those contaminated by radioactive substances and can be used for transportation and disposal safely.

(4) A device, such as a hood and glove box, connected to exhaust facilities shall be provided to prevent the spread of air contaminated by gaseous radioactive substances or radioactive substances.

F. There should be a contamination inspection room conforming to the following requirements (room for inspection and removal of contamination by radioactive substances on the surface of human body or objects worn on human body such as work clothes, shoes, and protective equipment; the same shall apply hereinafter). This does not apply to handling of radioactive substances in quantity or concentration at or below the levels specified by the Minister of Health, Labour and Welfare.

(1) It is installed in the most appropriate place for inspection and removal of contamination by radioactive substances (e.g., near the entrance of work area where people always enter and leave).

(2) The requirements of (1) and (2) of E shall be met.

(3) Cleaning facilities and gowning facilities are provided, and radiation measuring instruments for inspection of contamination and equipment necessary for removal of contamination are provided.

(4) The drainage pipes of the cleaning facilities specified in (3) are connected to drainage facilities.

[3] Storage facilities conforming to the following requirements shall be provided.

A. A main structure, etc. is fireproof, and a storage room with a fire door or storage box with a fireproof structure is provided at the opening.

B. Shielding walls and other shielding items conforming to the standards of C of the preceding item are provided.

C. There shall be only one entrance/exit site, where people enter/leave on a routine basis.

D. There should be a key or other facility or apparatus for closure at a part, such as a door and lid, leading to the outside.

E. There should be a lockable facility or apparatus for storing radiopharmaceuticals separately from the other goods.

F. There should be containers for radioactive substances conforming to the following requirements.

(1) Containers for radioactive substances that may contaminate the air outside the containers should have an airtight structure.

(2) Containers of liquid radioactive substances should have a structure to prevent liquid spill and be made of materials that are unlikely to be penetrated by liquid.

(3) For containers of liquid or solid radioactive substances, which may cause accidents, such as cracks and breakage, trays, absorbent materials, and other facilities or apparatuses shall be provided to prevent the spread of contamination by radioactive substances.

[4] A disposal facility conforming to the following requirements shall be provided.

A. They should be clearly separated from the other facilities.

B. A main structure, etc. is fireproof or made of non-combustible materials.

C. Shielding walls and other shielding items conforming to the standards of C of Item 2 are provided.

D. Exhaust facilities conforming to the following requirements shall be provided. This does not apply to cases where radioactive substances are handled in quantity or concentration at or below the levels specified by the Minister of Health, Labour and Welfare or cases where establishment of exhaust facilities significantly hinders the purpose of use or is difficult due to the nature of operations and there is no risk that gaseous radioactive substances are generated or that the air is contaminated by the radioactive substances.

(1) It is capable of keeping the concentration of radioactive substances in exhaust air at an exhaust port at or below the concentration limit specified by the Minister of Health, Labour and Welfare, or it is capable of keeping the concentration of radioactive substances in the air outside at the boundary (boundary of an area if measures are taken to prevent people from entering the area adjacent to the boundary of the registered manufacturing site without reason; the same shall apply hereinafter in this item) of a registered manufacturing site at or below the concentration limit specified by the Minister of Health, Labour and Welfare by

installing an exhaust air monitoring system and monitoring the concentration of radioactive substances in the exhaust air. This does not apply to the following case: It is significantly difficult to install exhaust facilities with such capability, and the exhaust facilities have the capability of keeping the dose, to which persons outside the boundary of a registered manufacturing site, at or below the dose limit specified by the Minister of Health, Labour and Welfare. The capability has to be approved by the Minister of Health, Labour and Welfare.

(2) The structure prevents gas leakage, and corrosion-resistant materials are used.

(3) There should be facilities that can prevent the spread of air contaminated by radioactive substances quickly in case of malfunction.

(4) It is capable of keeping the concentration of radioactive substances in the air in areas, where people enter on a routine basis, in work rooms, testing rooms, or disposal rooms (rooms where incineration residues of radioactive substances or materials contaminated by radioactive substances are taken out from an incinerator or solidified with concrete or other solidifying materials [including treatment for solidification; the same shall apply hereinafter]; the same shall apply hereinafter) at or below the concentration limit specified by the Minister of Health, Labour and Welfare.

E. In cases where liquid radioactive substances or solutions contaminated by radioactive substances are cleaned or discharged, drainage facilities conforming to the following requirements shall be installed.

(1) It is capable of keeping the concentration of radioactive substances in drainage at a drainage port at or below the concentration limit specified by the Minister of Health, Labour and Welfare, or it is capable of keeping the concentration of radioactive substances in drainage at the boundary of a registered manufacturing site at or below the concentration limit specified by the Minister of Health, Labour and Welfare by installing a wastewater monitoring system and monitoring the concentration of radioactive substances in drainage. This does not apply to the following case: It is significantly difficult to install drainage facilities with such capability, and the drainage facilities have the capability of keeping the dose, to which persons outside the boundary of a registered manufacturing site, at or below the dose limit specified by the Minister of Health, Labour and Welfare. The capability has to be approved by the Minister of Health, Labour and Welfare.

(2) The structure prevents leakage of drainage, and materials that prevent penetration of drainage and that are corrosion-resistant are used.

(3) A wastewater-purifier tank shall have a structure capable of collecting drainage or measuring the concentration of radioactive substances in the drainage and be equipped with a device to control the outflow of drainage.

(4) The opening at the top of the wastewater-purifier tank shall have a structure with a lid or

have a fence around it or other facilities to prevent unauthorized entry.

F. If radioactive substances or materials contaminated by radioactive substances are incinerated, exhaust facilities meeting the provisions of D, disposal room meeting the provisions of (1), (2), and (4) of E of Item 2, contamination inspection room meeting the provisions of (1) to (3) of F of the same item, and incinerator meeting the following requirements shall be provided.

(1) The structure should prevent gas leakage and ash scattering.

(2) It is connected to exhaust facilities.

(3) The outlet for incineration residue is connected to a disposal room.

G. If radioactive substances or materials contaminated by radioactive substances are solidified using concrete or other solidifying materials, exhaust facilities meeting the provisions of D, disposal room meeting the provisions of (1), (2), and (4) of E of Item 2, contamination inspection room meeting the provisions of (1) to (3) of F of the same item, and solidifying facilities meeting the following requirements shall be provided.

(1) The structure should prevent leakage or spill of radioactive substances or materials contaminated by radioactive substances and dispersion of dust.

(2) Materials that prevent penetration of liquid and corrosion are used.

H. If radioactive substances or materials contaminated by radioactive substances are stored and disposed of, storage and disposal facilities conforming to the following requirements shall be installed.

(1) The structure shall be separated from the outside.

(2) There should be a key or other facility or apparatus for closure at a part, such as a door and lid, leading to the outside.

(3) Containers (those with fireproof structure only) conforming to the provisions of the preceding item are provided.

[5] At the boundary of controlled areas specified in Item 3, Article 1 of the Regulations for Manufacturing and Handling of Radiopharmaceuticals, facilities, such as fences, shall be provided to prevent unauthorized entry by other persons.

2. If exhaust facilities or drainage facilities approved based on D (1) or E (1) of Item 4 of the preceding paragraph are no longer considered to have the capability to be approved, the Minister of Health, Labour and Welfare may revoke the approval.

3. The provisions of Item 1, B to E of Item 2, A to D and F of Item 3, Item 4, and Item 5 of the preceding paragraph shall not apply to cases where only radioactive substances are handled in amount or concentration at or below the levels specified by the Minister of Health, Labour and Welfare.

(Compliance with regulations for manufacturing and handling of radioactive *in vitro* diagnostics)

Article 81 In addition to the provisions of the preceding article, marketing authorization holders, etc. of products related to radioactive *in vitro* diagnostics shall verify that registered manufacturing sites are conducting operations based on the provisions of the Regulations for Manufacturing and Handling of Radiopharmaceuticals.