Development of a Local Clean Chamber for the Production of Radiopharmaceuticals

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1. Introduction

In order to operate a hot cell for producing radiopharmaceuticals, both the Atomic Energy Safety Act and the Pharmaceutical Affairs Act [1] must be satisfied, so radiation safety as well as internal cleanliness management must be secured. However, the hot cells built in the HANARO RIPF, a research reactor of the Korea atomic energy research institute, were completed decades ago. At that time, there were no provisions regarding hot cells related to the Pharmaceutical Affairs Act, so construction was completed considering only the regulatory standards under the Atomic Energy Safety Act. In order to use radioisotopes produced in HANARO for medical purposes, the use of these hot cells is inevitable, but it is difficult to secure cleanliness standards in the state at the time of construction, making it difficult to use them. In addition, even if the hot cell structure is changed, it is very difficult to obtain permission for change and perform construction due to the nature of the facility included in the reactor auxiliary facility. Since one of the main functions of HANARO is the "supply of radioisotopes" it is necessary to devise a plan to utilize the aging hot cells as a production facility for medical radioisotopes and radiopharmaceuticals. Accordingly, in this study, we developed a technology that can create a clean environment as stipulated in the Pharmaceutical Affairs Act without direct structural changes or improvement work for hot cells that are aged and difficult to meet the cleanliness standards. We completed the development of equipment that creates a clean environment locally inside the hot cell, enabling the existing hot cell to be used for pharmaceutical production.

2. Purpose and Challenges to be solved

We performed technology development for carrying out the radiopharmaceutical production process in an aged hot cell where cleanliness standards were not considered at the time of construction. First, we derived the cleanliness requirements of the hot cell by considering the production process of the radiopharmaceutical I-131 mIBG currently in production. Since an aseptic work environment is not required until the filtration sterilization stage among the series of production processes, it was reviewed that the process could be performed using the currently constructed hot cell. However, the distribution process performed after the filtration sterilization stage must be performed in an aseptic environment. According to the Pharmaceutical Affairs Act, the aseptic environment in which the distribution process is performed must satisfy Grade A.

In order to create a local clean environment, we first performed actual space measurements required for the process to be performed. As a result of the measurements, we derived the conditions that a width of 50 cm and a depth of 40 cm are required, and that the internal height of the chamber must be secured at least 55 cm when considering the height of the equipment performing the distribution process. The distribution process is performed by installing equipment inside the hot cell and using a remote operator called a robot arm outside the hot cell. Accordingly, the chamber should be manufactured to facilitate operation with a remote operator for actual use in the process, so the front of the chamber was designed to allow easy viewing of the inside and easy operation through entry of the remote operator. In addition, in order to maintain air flow inside the chamber during the process, the front cannot be completely opened, so the height was fixed to allow for opening in stages. The chamber size was designed to be 60 cm · 47 cm · 60 cm (W · D · H). It would be nice if the space inside the chamber was secured as large as possible, but the chamber must be installed through the hot cell door, so the size was determined considering this. A fan filter unit was installed on the top of the chamber to allow clean air to be introduced into the chamber at a rate greater than the number of ventilation cycles stipulated by the regulations. Since the chamber is installed inside the hot cell, it may affect the supply and exhaust volume of the existing hot cell. However, the supply and exhaust of the hot cell is determined by the entire building's air conditioning system, and any changes to this may require work such as changes to permits. Therefore, an air circulation system for the internal air was applied to prevent changes in the supply and exhaust of the hot cell due to the chamber. Perforations were installed in the lower floor of the chamber to allow internal air to circulate, and an air vent was placed on the side of the chamber to allow air drawn in from the bottom to move upward. In addition, a pipe was installed to connect the upper part of the chamber where the air vent is installed and the part where air is drawn into the fan filter unit, so that the air inside the chamber passes through the fan filter unit and is drawn back into the chamber. In this case, the supply and exhaust of the entire hot cell is not

affected, so the design was performed so that it can be used without additional permits for changes..

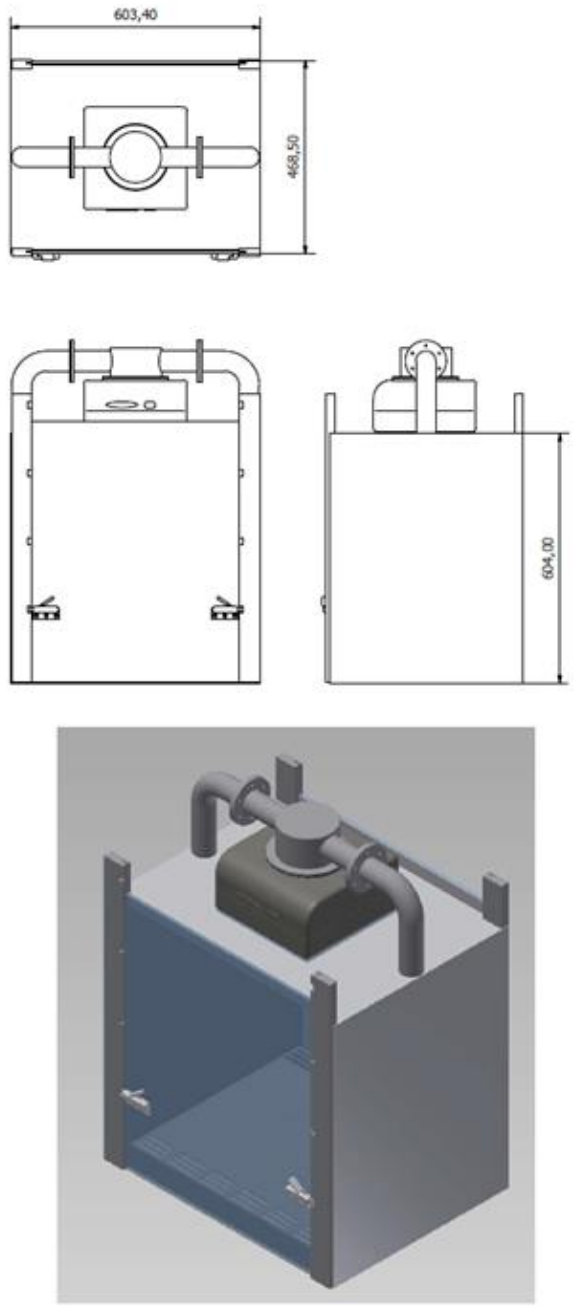

Fig. 1. The design of clean chamber

3. Results and Conclusions

In the case of the currently constructed hot cell, considering the number of ventilation cycles that can secure performance, only up to a C grade can be secured, so in order to secure an A grade, the hot cell structure had to be changed or the number of ventilation cycles had to be sufficiently increased to improve the conditions. However, if the structure of the hot cell belonging to the reactor auxiliary facility is changed or the ventilation cycle inside the hot cell is adjusted by changing the air conditioning of the entire building, the approval process such as structural safety verification and radiation environmental impact assessment must be completed, and the process requires a lot of manpower, time, and money, so it was realistically impossible to perform the work only for the purpose of structural change of the hot cell. Accordingly, in order to create an A grade environment while maintaining the structure of the hot cell and the amount of air supplied and exhausted, the development of a clean chamber that can only locally satisfy the conditions was completed, giving up the use of the entire hot cell interior space. As a result of the test operation, it was confirmed that the inside of the chamber maintained an A grade environment as specified in the pharmaceutical manufacturing environment standards. Through this, the already constructed hot cell could be used for the production of radioactive pharmaceuticals.

REFERENCES

[1] Guidance on Good Manufacturing Practice(GMP) for Radiopharmaceuticals, Ministry of Food and Drug Safety, 2014.