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Integrity Test for Hepa Filters in Cleanroom Preparation and Cleanroom Process of Labeled Compound

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Abstract

One of some factors that take effect for the cleanroom sterilization is the integrity of HEPA filters. The value of HEPA filters integrity should be contained in the qualification document of air conditioning system (HVAC). HEPA filters integrity testing aims to ensure the performance of HEPA filters that installed in the air conditioning system, so that no leakage occurs in the installation of HEPA filters, that cause the cleanroom becomes unsterile. The methodology used is to supply aerosol concentration in the upper HEPA filter between 10 - 100 µg/L, and then perform a maximum aerosol penetration measurement on the downstream of HEPA filter. The results are compared with the standard provisions that is contained in the "Procedural Standards for Certified Testing of Cleanrooms", where the maximum permissible penetration is 0.01%. The maximum value of aerosol penetration below 0.01%, that states a HEPA filter has good integrity. While the maximum value of aerosol penetration percentage above 0.01%, states that a HEPA filter has poor integrity. Integrity test of HEPA filters was performed on 8 units, there are in the cleanroom preparation and cleanroom process of labeled compound. The result obtained from the test is that all HEPA filter units have excellent integrity with maximum penetration percentage below 0.01%. The maximum aerosol penetration rate obtained from the overall HEPA filter is 0.004825 % ± 0.000707.

Keywords: Labeled Compound, Cleanroom, HEPA filter integrity, Aerosol penetration

1. Introduction

In the process of making radiopharmaceutical medicine requires cleanroom as the main facility [1]. The cleanroom function is as a sterilization facility, that guarantees the product is free from particles and other microbes [2]. Furthermore, the sanitary of ingredients that used to make medicine need to be maintained, so that they are not contaminated by microbes, that can change the substance content in the medicine to be dangerous if consumed [3]. The air conditioning system is one of the facilities that effect the cleanroom sterility. In the air system, there is an important component in the form of High Efficiency Particulary Air (HEPA) filters which have function to filter particles and microbes so that cleanroom becomes sterile[4]. National Nuclear Energy Agency (Batan), especially Center for Radioisotope and Radiopharmaceutical (PTRR), has obtained certification of Good Manufacturing Practices (CPOB) from the Food and Drug Supervisory Agency (BPOM). In order to maintain this certification, Batan-PTRR always strives to fulfill all the terms and conditions that stipulated through the CPOB Guidelines for Implementation (POPP). Includes provisions for qualifying the air conditioning system with various criteria of acceptability. These criteria include; room temperature (18°C-22°C), Humidity (40%-55%) and number of particles (according to class).

In the POPP mentioned that the HEPA

filters integrity have good value. This value is proven by the maximum percentage of aerosol penetration that can be measured using a photometer measuring instrument and then be compared with the acceptance criteria required in the Procedural Standards for Certified Testing of Cleanrooms [5]. Therefore, in this research the HEPA integrity test is carried out in cleanroom preparation and cleanroom process of labeled compounds.

2. Materials and Methods

2.1. Materials and Equipment

In HEPA filter integrity testing, the following materials and equipment are needed; HVAC system of Cleanrooms, 8 unit of HEPA Filters have been installed in the cleanroom preparation and cleanroom process of labeled compounds, ATI-2i model of ATI Photometer that used to measure aerosol penetration, Velocity meter TSI Probe 966 which is used to measure the velocity of air flow at outlets HEPA filters, Aerosol Generator (ATI TDA 4B) and Challange Agent Aerosol (ATI PAO-5 Gal) is used to make aerosol concentrations and then penetrate to the inlets of HEPA filters [6].

2.2. Methodology

The methodology used in HEPA filters integrity testing is to supply aerosols in the HEPA filters inlet and then measure the maximum percentage of penetration [78]. In the implementation, several activities were carried out such as HEPA filter inspection which aimed to ensure that there was no leakage outside the HEPA filter area. The inspection activity is carried out by tightening the reinforcing bolt and adding a sealent to the edge of the HEPA filter frame. Then measurements of air flow velocity at HEPA filter output with a requirement value between **0.40 m/s - 0.50 m/s**. The next step was to supply aerosols at the HEPA filter inlet and then scan the measurements at the HEPA filter outlet. Aerosol concentration (Upstream Concentration) must be in the range between 10 ug/L and 100 ug/L according to the requirements specified. Maximum aerosol penetration measurements were carried out using a Photometer with a scaning speed of around 5 cm/s and the measuring instrument was 1 inch below the HEPA filter area [9]. The movement of measuring instruments is carried out as shown in Figure 1. Data obtained from the Photometer measuring instrument is in the form of average data in one scanning period of measurement with percent units (%). Requirements submitted in National Environmental Balancing Bureau Third Edition, that the maximum penetration percentage of aerosols required is not exceeding 0.01%.

3. Results

3.1. Checkout the HEPA filters installation

In the inspection of installation for HEPA filters, found leaks on gaskets or seals of HEPA filters units have been installed, both in the cleanroom preparation and in the cleanroom process of labeled compound. The corrective action taken is to remove the HEPA filters unit, then add or replace the gaskets or seals and then reinstall the HEPA filters

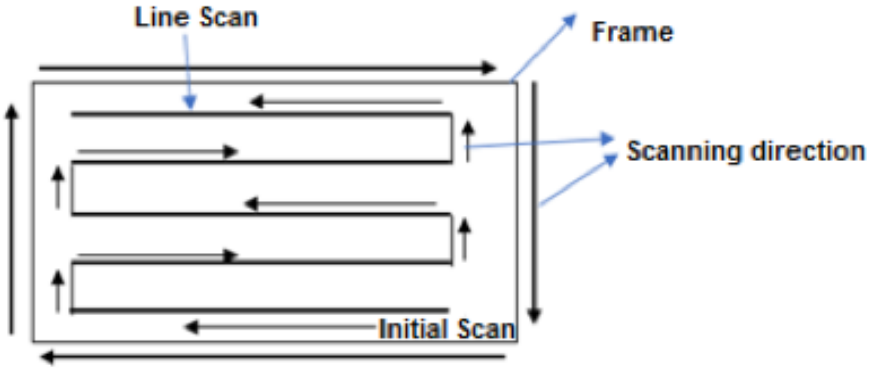

Figure 1. The direction of movement of the Photometer measuring instrument in HEPA filter integrity testing

and make sure the locking bolts are firmly attached. Then leak test is performed on the gaskets or seals to ensure that the gaskets or seals does not leak. The test was carried out by giving aerosols on the edge of the filter unit and scanning with the ATI Photometer (ATI-2i Model). The results obtained are no more leaks in all HEPA filters installations in the cleanroom preparation and in the cleanroom process of labeled compound. Furthermore, HEPA filter integrity testing can be carried out.

3.2. Measurement of airflow velocity

Airflow velocity is measured at the output of each HEPA filter [10]. Measurements are carried out at a distance of 15 cm below the surface of the HEPA filter. In each HEPA filter measurements are taken 8 points were measured as shown in the measurement layout in Figure 2. Results of airflow velocity measurements can be seen in Table 1.

3.3. Integrity Testing for HEPA Filter in Cleanroom Processes Labeled Compound

The integrity test is carried out by penetrating aerosols into each of the HEPA filter inlets in the cleanroom process of labeled compound. Layout of HEPA filters in the cleanroom process of labeled compound can be seen in Figure 3.

Data for integrity test of HEPA filter cleanroom process of labeled compound can be seen in Table 2.

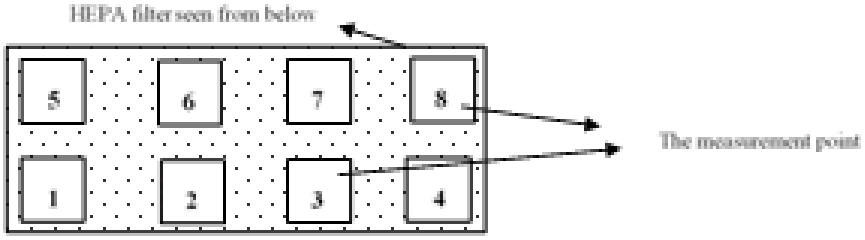

Figure 2. The measurement point on each HEPA filter

Table 1. Airflow velocity measurements in the cleanroom process and in the cleanroom preparation of labeled compound.

No	HEPA filter	The Measurement point of Airflow velocity (m/s)								Average (m/s)
		1	2	3	4	5	6	7	8	
1	Process 1	0.46	0.47	0.45	0.47	0.47	0.46	0.45	0.44	0.46 ± 2.45 %
2	Process 2	0.47	0.47	0.46	0.45	0.46	0.47	0.46	0.45	0.46 ± 1.81 %
3	Process 3	0.44	0.45	0.44	0.43	0.45	0.44	0.43	0.45	0.44 ± 1.89 %
4	Process 4	0.45	0.45	0.46	0.45	0.44	0.44	0.46	0.46	0.45 ± 1.85 %
5	Preparation 1	0.47	0.45	0.45	0.46	0.47	0.46	0.46	0.45	0.46 ± 1.82 %
6	Preparation 2	0.43	0.45	0.44	0.43	0.46	0.44	0.45	0.45	0.44 ± 2.39 %
7	Preparation 3	0.46	0.47	0.44	0.45	0.45	0.44	0.46	0.45	0.45 ± 2.29 %
8	Preparation 4	0.45	0.47	0.44	0.46	0.45	0.44	0.45	0.46	0.45 ± 2.29 %

3.4. Integrity Testing for HEPA Filter in Cleanroom Preparation Labeled Compound

The integrity test in the cleanroom preparation of labeled compound is carried out by penetrating aerosols into each of the HEPA filter inlets. Layout of HEPA filters in the cleanroom preparation of labeled compound can be seen in Figure 4. While the data for integrity test of HEPA filter cleanroom preparation of labeled compound can be seen in Table 3.

4. Discussion

Inspection and repair of installations HEPA filters have been carried out and provide good results, that is no more leakage on gaskets or seals of HEPA filters. The next step is Air velocity measurement can be carried out. Based on Table 1, the air flow velocity values for each HEPA filter have met the acceptability criteria that is 0.36 m/s - 0.54 m/s as stated in the Procedural Standards for Certified Testing of Cleanrooms. Therefore, all HEPA filters in the cleanroom preparation

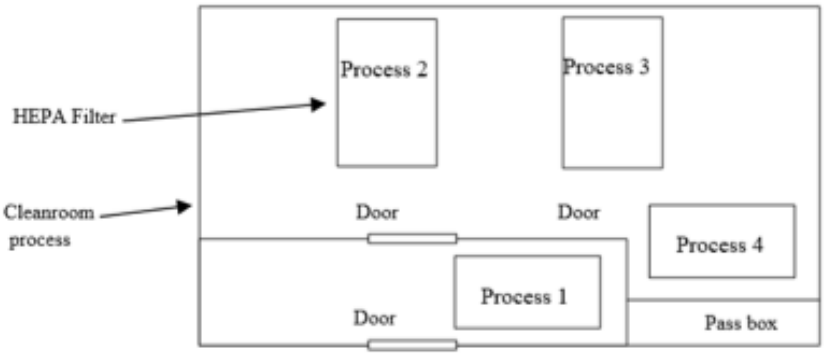

Figure 3. HEPA filter layout in the cleanroom process of labeled compound

Table 2. Result for aerosol penetration at each HEPA filter in cleanroom process of Labeled Compound.

No.	HEPA Filter	*Upstream Concentration* (ug/L)	*Acceptance criteria* (%)	*Max Downstream Penetration* (%)	*Result (Pass/Fail)*
1.	Process 1	29	0.01	0.0040	*Pass*
2.	Process 2	20	0.01	0.0070	*Pass*
3.	Process 3	17	0.01	0.0081	*Pass*
4.	Process 4	88	0.01	0.0022	*Pass*
			Average	**0.005325 ± 0.00271**	

and cleanroom process of labeled compound can be carried out aerosol penetration for HEPA filter integrity measurements. Tables 2 and 3 show the results of aerosol penetration in each HEPA filter in the cleanromm preparation and the cleanroom process of labeled compound. The position of the HEPA filter is in the cleanroom process as shown in Figure 3. In the cleanroom process, aerosol penetration data were 0.0040%, 0.0070%, 0.0081% and 0.0022% respectively. The averege of aerosol penetration data are 0.005325% ± 0.00271. All of these values are below 0.01% so that it is in accordance with

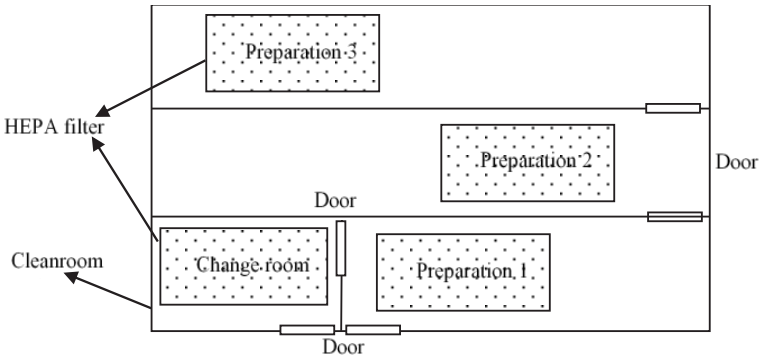

Figure 4. HEPA filter layout in the cleanroom preparation of labeled compound

Table 3. Result for aerosol penetration at each HEPA filter in cleanroom preparation of Labeled Compound.

No.	HEPA Filter	Upstream Concentration (ug/L)	Acceptance criteria (%)	Max Downstream Penetration (%)	Result (Pass/Fail)
1.	Change Room	68	0.01	0.0025	*Pass*
2.	Preparation 1	33	0.01	0.0031	*Pass*
3.	Preparation 2	65	0.01	0.0053	*Pass*
4.	Preparation 3	15	0.01	0.0064	*Pass*
			Average	**0.004325 ± 0.00183**	

NEBB (National Environmental Balancing Bureau) and therefore HEPA filters are declared to have good integrity.

Likewise, the position of the HEPA filters is in the cleanroom preparation as shown in Figure 4. The aerosol penetration data carried out on the HEPA filters in the cleanroom preparation as shown in Table 3, the values in a row 0.0025%, 0.0031%, 0.0053% and 0.0064%. The average of aerosol penetration data are 0.004325 % ± 0.00183. This value is also in accordance with the standard value provided by NEBB which is under 0.01%. Therefore, HEPA filters installed in the cleanroom preparation are declared to have good integrity. The average of Maximum Downstream Penetration of cleanroom preparation (0.004325% ± 0.00183) and cleanroom process (0.005325% ± 0.00271) then obtained a maximum average aerosol penetration in cleanroom labeled compounds at 0.004825% ± 0.000707.

5. Conclusion

All HEPA filters in the cleanroom preparation and cleanroom process of labeled compounds have a maximum downstream penetration rate below 0.01% with an average of all HEPA filters at 0.004825 % ± 0.000707, thus the condition of the HEPA filter is declared feasible to operate in order to support the implementation of production process of the labeled radiopharmaceutical compound. Furthermore, it is expected that this method can be used to test the other HEPA filters before being used to support the production process.

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