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Studying and simulation of clean area for Tc^{99m} production in Radioisotope Production Facility

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ABSTRACT

Clean areas nowadays are advanced technology solutions with very high standard and criteria applied on air quality level. Egyptian Radioisotopes Production facility (RPF) is a facility that requires clean area to produce technetium (Tc^{99m}) isotope for medical purposes. The air cleanliness inside area is dependent on the air quality of supplied air, contaminant and pollutant sources, dedicated ventilation system in addition to rigorous precautions to sterilize space of the area and commitment to follow standard recommendations. Two main standard classes are available in production area, A and C according to ISO 14644-1. Our paper deals with class C in which isotope is produced and some tests are conducted to know particle counts in that area in addition to prediction of these counts by computer simulation Contam-CFD0 program, which predicts transient particles count behavior which compared with standard WHO values and measurements for validation. Biological tests are also implemented to monitor sterility of area to confirm cleanliness and validity for processing medical radioisotope. High efficiency particulate air filters with class H14 are dedicated for the clean area and equipped with pressure drop manometer for replacement in case of blockage. Simulation program is also used to predict particles concentration in case of filter contamination.

Nomenclature

V	Volume of the clean area, m^3
C	Particle concentration in clean area, particles.m^{-3}
Q	Inlet fresh air flow rate, $m^3\ s^{-1}$
Q	Leakage air flow rate to area, $m^3\ s^{-1}$
S	Generated particle, p s^{-1}
E	contaminant removal effectiveness factor
T	Time, s
X	fraction
K	Constant
H	Efficiency
Cfu	Colony forming unit
FFU	Fan filter unit
LES	Large Eddy Simulation

Subscripts

Exit	Exhaust (exit) air from the clean room
S	Source
In	Inlet
out	Outlet
Re	Recirculated air
S	Supplied air
L	Leakage
0	Initial

1. INTRODUCTION

Clean area is an area proposed for manufacturing special products or scientific research that has a minimum amount of environmental pollutants or particles where it has a level of contaminants under control. Clean room in RPF facility has class C, which we study to verify its validity to produce radio pharmaceutical product, (Tc^{99m}) as well as to be compliance with regulations of ministry of health. It should follow also WHO standard for particles count as well as microbial count. In nuclear application environments where radioactive materials are manipulated there are always a probability of accidental and unintentional airborne releases of toxic or radioactive substances in form of noble gases or aerosols. Understanding the air flow movement and aerosol trajectories in ventilated rooms can guide us to understand and determine where correctly place early detectors for warning and monitoring, and how to minimize risk from hazardous materials in the worker's environmental area. In particular, with the mathematical modeling the capabilities of the mathematical model is

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firstly evaluated to reproduce the available experimental data and secondly defined a way for localization of permanent air monitoring detector to get a quickly and good sensitive feedback [1]. Good ventilation system can play role to minimize the cooling energy consumption of buildings, enhancing comfort level of residence, and reducing the risk probability of airborne infection in hospital rooms. Ventilation in a hospital room deeming ventilation with forced and natural regime, and the trajectory of bacteria particles released from a patient are predicted using CFD software [2]. With these types of software it can be gotten better recognition into aerosol contamination release and dispersion characteristics to justify airflow movements in clean rooms in hospitals. Deposition of airborne particles onto cleanroom surfaces is discussed [3]. It is investigated the relationship between particle deposition rate (PDR) and airborne concentration of a range of cumulative sizes of particles onto cleanroom surfaces, through defined particles deposition velocity in air. The deposition velocity was obtained by experimental means, theoretically by calculations, and literature survey and the effect of some parameters available in cleanrooms on the deposition velocity was studied. Deposition velocity is used to model the quantity of deposition and concentration on cleanroom surfaces, such as proposed products is discussed and investigated along with its use in defining the required ISO 14644-1 class of cleanroom. C. Y. Chuah [4] analyzed, simulated, and compared two types of non-unidirectional clean rooms which are also defined as locally balanced and wall return turbulent clean rooms, by CFD analysis. Comparison was made between all the different turbulence models to determine which set of these models is acceptable for the clean area modeling. Large Eddy Simulation, (LES) model showed clearly various results where it is thank that LES model have more accuracy. The mathematical model derived by Whyte, e tal [5] showed that the variables that influence the re-dispersion factor, or airborne concentration in a room, are the total walking activity, re-dispersion fraction, shoe area, air supply rate, and deposition on surfaces. The concentration of microbes on the floor has no effect on the re-dispersion factor but is required in order to calculate the airborne microbial concentration of floor microbes. Re-dispersion factors were calculated for microbe-carrying particles, (MCPs) in a range of conditions found in a different operating cleanrooms. Over the range of conditions explored in cleanrooms, when the surface concentration was measured by special types of plates and the percentage ranged from 0.004% to 10.5% . In a typical operating room, the percentage of floor-derived microbes in the operating room air was found to be 2, and in a typical pharmaceutical cleanroom, it was 0.7.

Fluent CFD software is employed to model flow of air from fan filter units into and out of the micro environment of a welding automation machine of a hard disk drive production line to consider its airborne particle purging and blocking capabilities [6]. It was concluded that the airflow from the Fan Filter Units (FFUs) was able to block out particles effectively when the FFUs' air speed was in the range of 0.25-0.65 m/s. The airflow can also purge out internally generated particles effectively. However, at higher air speed, the airflow pushed more particles onto the conveyor, contaminating it more instead. The overall optimum FFUs' air speed, for both the particle blocking and purging purposes was shown between 0.35-0.55 m/s.

In this study a mathematical model is formulated to predict particle count of clean area during startup the ventilation system till the steady state condition, while the CFD analysis is presented to illustrate the concentration of these particles in the area. Measurements are also conducted to verify clean room class according to WHO standard.

2. Radio Isotopes Description

The facility consists of many hot cells which are used to handle radioisotopes. Molybdenum 99 (Fission) production hot cells contain four hot cells where Mo-99 sodium molybdate solution is produced. Iodine-131 production hot cell which produce Iodine-131 as carrier-free solutions of high activity concentration that allow their further fractionation and capsulation for use in nuclear medicine as therapeutic and diagnosis agent, and to label other compounds of interest. Hot cell to produce I-125 solution for use in nuclear medicine as therapeutic and diagnosis agent, and to label other compounds of interest. Chromium 51 production hot cell to produce aqueous Cr-51 enriched sodium chromate solution for use as injectable medical product. Iridium 192 production hot cell that composed of two hot cells to obtain Ir-192 wires for use in medicine and Ir-192 sealed sources for use in industrial gamma radiography. Assembly and loading of the Technetium generator hot cell dedicated to the loading of the Molybdenum 99– Technetium 99m (GENTEC) generator. Multi-purpose production hot cells which proposed for compound labeling or production of other radioisotopes and activity control hot cell which allows radionuclide calibration and activity control prior to dispatch. Hot cells are airtight boxes fitted with a ventilation system with air filters at its inlet and outlet, connected to the

central ventilation system. Process equipment, glove boxes, laboratories, and radiochemical hoods were distributed inside the facility with a view to ensuring comfortable working conditions and minimum personnel circulation. Moreover, teletongs and master-slave manipulators are supplied to handle isotopes safely by operators. The hot cells have auxiliary services such as compressed air, vacuum, and liquid effluent collection.

3. Ventilation system description

The dedicated ventilation system is proposed to satisfy class 10,000 in loading area. This requirement is satisfied by Air treatment unit (ATU) in supply line with its own pre and absolute filters. While Hepa filters with class H14 are dedicated in supply line just before entering the area. Exhausted air in range of 85% is permitted to recirculate to ATU again. The system receives 15% of outside air, which is sucked by air treatment mixed with the recirculation current. The air is then filtered, conditioned, and further driven to the rooms. The surplus air is released into the hot corridor through closing damper, which closes when air treatment unit is not operating. The room is depressurized with respect to the outside. The defined depressurization steps are aimed at preventing cross contamination between the rooms, and at ensuring that any eventual leak is driven towards the hot corridor

4. Mathematical model

The air cleanliness level in any clean area is dependent on the quality of the entering air, contaminant sources and design of the dedicated ventilation system. It is not easy to estimate the final cleanliness class, but it can be achieved either by using mathematical approach or by experimental investigation. The most effective and fastest approach is to use analysis by computer. Contam with computational fluid dynamic (CFD0) [7] are employed to calculate airflow patterns, streamline movements and also in analyzing the particles dispersion. This type of software application helps the designer and researcher to predict the cleanliness class in these rooms using many types of air filters. Depending on the number of people and activities in the room, the ventilation system and the filter selection, so the clean room class is calculated.

4.1 Mass flow balance

A clean room is dependent on having a balance between inlet and outlet air flow rate in order to minimize contamination from supplied air to room as well as having an effective removal of any contamination generated inside the room (processes, accidents, human activity etc.). The mass flux law governs the airflow balance is:

$m_{in}= m_{out}$, where m is the mass flow rate.

4.2 particulate balances

The level of particles in air contaminants of any area of interest is estimated by the quantity of particles that entered and extracted from the area. However, particle sources inside the area arise from people and garments they use. Any particles result from the process, people or other activities cause more concentration inside the area. Correct dedicated air filters can efficiently increase the cleanliness level. Additional precautions are required to develop classification of it and can use recirculation of air through theses filters for the whole room, employing outlet grills close to contaminant sources and improve the clothing on the people working in the area. In order to model mathematically the linkage between the design of ventilation system, source of particles and dedicated filters to get results of particle concentration, C (t). Fig. 1 illustrates the flow rate and particulate balance in the room with the volume (V). The air supplied to area is defined by (Q) $m^3 s^{-1}$ and the re-circulated air flow rate is (x.Q) $m^3 s^{-1}$, where (x) is the part of the entered air which is "recycled" (x ranges from zero to 100%). The amount of extracted air flow equals (1-x).Q $m^3 s^{-1}$, and guides air filter (Filter, s) with the required efficiency (η_s) and a recirculating air filter (Filter, re) with the efficiency of ($\varepsilon.\eta_{re}$). The particle concentration of entering supply air (C_s) is what filters (s) have to remove. An infiltration to the room is defined (q) $m^3 s^{-1}$, having the leaked concentration, particles m^{-3} (C_L).

The ventilation effectiveness factor relies on the dedicated cleaning equipment, the dispersion of contaminants, its area and the position of the available sources. The below mathematical equations are formulated to define the balance of any particles in clean area, as illustrated in Fig.1.

Particles arise in the area according to:

Fresh air from outside: $(1-x)(1-\eta_s)*Q*C_s$ [particles.s^{-1}]

Air recirculation quantity: $x*(1-\eta_{rec})*Q*C(t)$ [particles.s^{-1}]

Infiltration (into clean area): q. C_L [particles.s^{-1}]

Generated particles: S [particles.s^{-1}]

The difference between quantity of particles extracted and entered to the area in time interval Δt will be affected and the concentration of the particles are changed by amount (ΔC). Any particles variation in the clean area is then expressed by $V*\Delta C$, where term V expresses clean area volume and can be formulated as[8]:

$$V.\Delta C = [(1-x).(1-\eta_s).Q.C_s + x.(1-\eta_s).Q.\varepsilon.C(t) + q.C_L + S - (Q+q).\varepsilon.C(t)]\Delta T \quad (1)$$

$$k_1 = E.Q.\left(1+\frac{q}{Q} - x\,(1-\eta_{re})\right) \quad (2)$$

If Δt approach zero equations 1, 2, 3 become

$$k_2 = (1-x).(1-\eta_s)\,Q * C_s + q * C_L \quad (3)$$

$$V.dC(t) = (S - k_1 * C(t) + k_2)\,dt \quad (4)$$

$$V\int dC = \int_{t_0}^{t} (S - k_1.C(t) + k_2)\,dt \quad (5)$$

$$V\int_{C_0}^{C} \frac{1}{(S - k_1.C(t) + k_2)}\,dC = \int_{t_0}^{t} dt \quad (6)$$

Integration of equation 6 gives

For t_0=0 and C=C_0 the next equations are gotten

$$t = \frac{V}{k_1}\ln\left(\frac{S + k_2 - k_1 * C}{S + k_2 - k_1 * C_0}\right) \quad (7)$$

$$C = \left(C_0 - \frac{S}{k_1} - \frac{k_2}{k_1}\right).e^{-\frac{k_1.t}{V}} + \frac{S}{k_1} + \frac{k_2}{k_1} \quad (8)$$

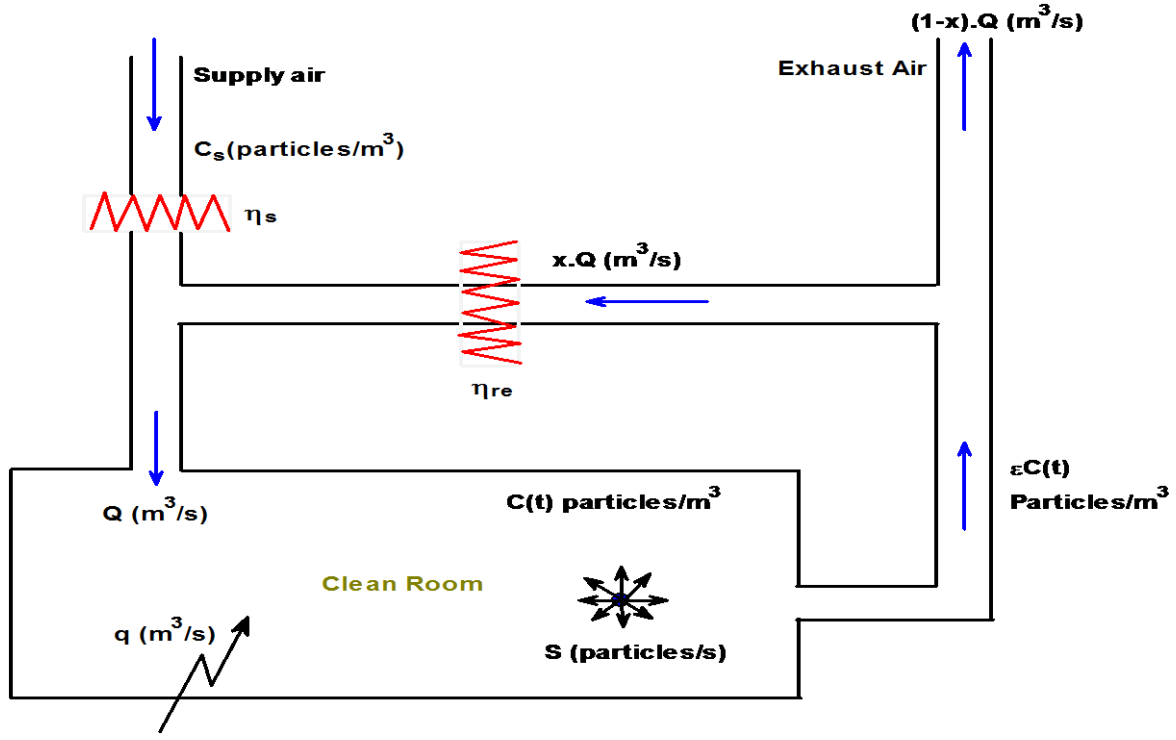

Fig. (1): Particles balance in clean room

As illustrated in the equations the concentration of particles consists of two parts. First part varies with time and second part does not rely on time. The part that depends on time is due to dilution of the particle concentration and is defined by inclination in concentration with time.

When time goes infinity the time dependent term will diminish, and thus this term disappears. This state represents a stationary clean room process which often is referred to as "the steady state condition". However, in many cases, it is important to assess transient state such as difference in internal particle generation or other time dependent stages.

Thus, for a stationary process (t approaches ∞) equation (8) becomes:

$$C_{\infty} = \frac{S}{k_1} + \frac{k_2}{k_1} \qquad \textbf{(9)}$$

The equations above can be simplified when one or more terms such as:

- Generation of internal particles is constant,

- Particle concentration outside (C_s) is considered also constant

- Concentration in leakage air (C_L) is already exists.

Ventilation effectiveness (ε) is defined how effectively the ventilation system removes contaminants. This factor is denoted also (Contamination removal efficiency).

$$\varepsilon = \frac{C_{out} - C_s}{C(t) - C_s} \qquad \textbf{(10)}$$

Where,

ε: is the system factor of effectiveness to remove contaminants;

C_s: is the concentration of particles in inlet air;

C(t) : is the particles concentration in a room at any time.

The Ventilation effectiveness factor ranges is tabulated.

Table (1): Typical ventilation system effectiveness factors for various clean areas configuration

Ventilation Efficiency	System	Example
$\varepsilon \rightarrow \infty$	Contaminant outside, the flow have no impacts.	Extraction is excellent as well supply air is clean.
ε = 1.0	Complete and instantaneous mixing. Contamination source does not have any effect.	Unidirectional clean area ventilation design.
ε = 0.70	Contaminants extraction is considered good.	Turbulent mixing clean area with good position of dedicated fans.
ε =0.30	Medium extraction level of contaminants from the area	Typical normal ventilating areas
$\varepsilon \rightarrow 0$	Source of contamination exists in the recirculation path as well as bypass of supply air	Short circuited system, with very poor dilution. Supply air will not help to reduce the concentration in the clean room

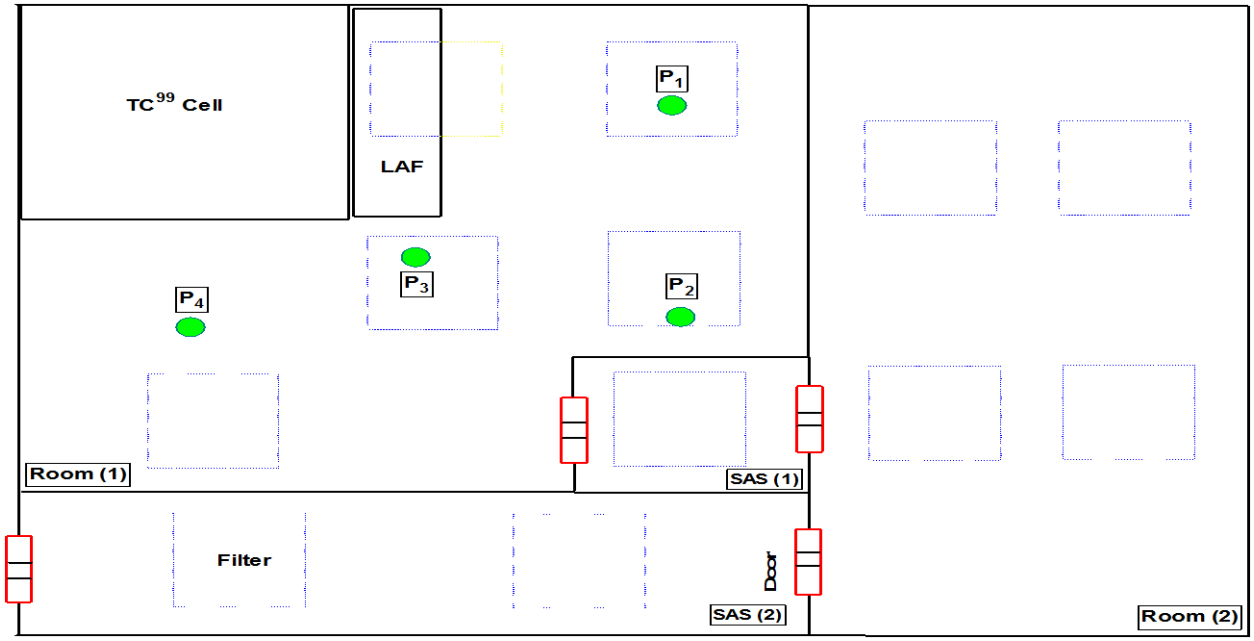

Fig. (2): Clean area layout and position of measurements

5. RESULTS AND DISCUSSIONS

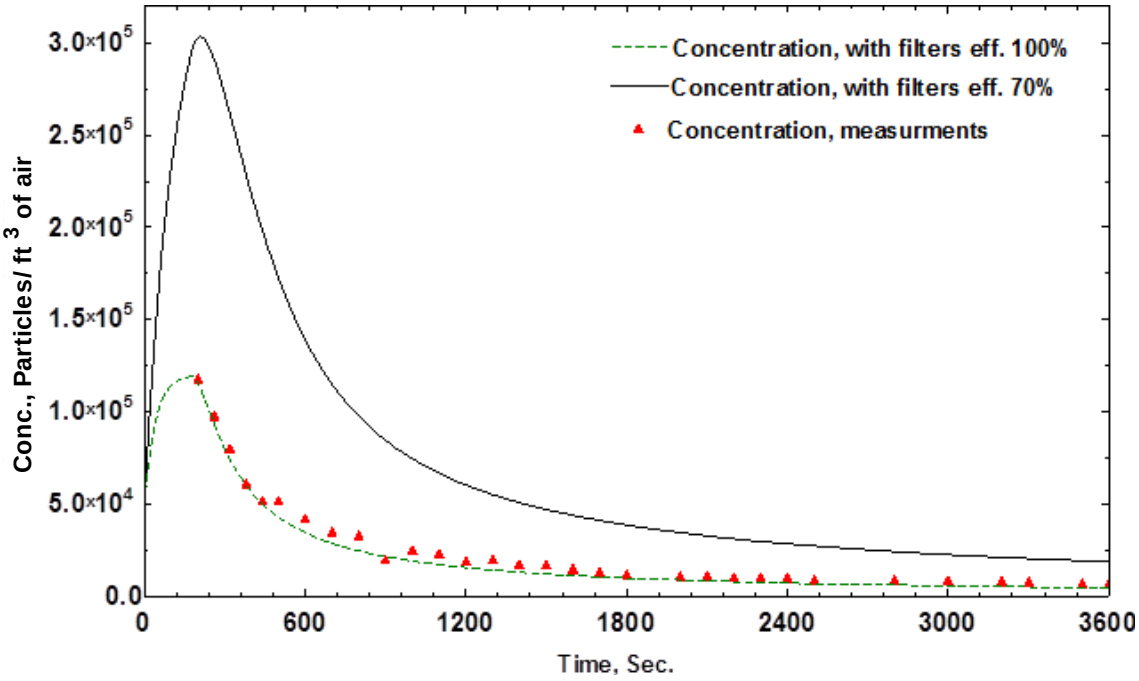

Fig. (3): Concentration with different filtration efficiency, 0.5 µm particle diameter

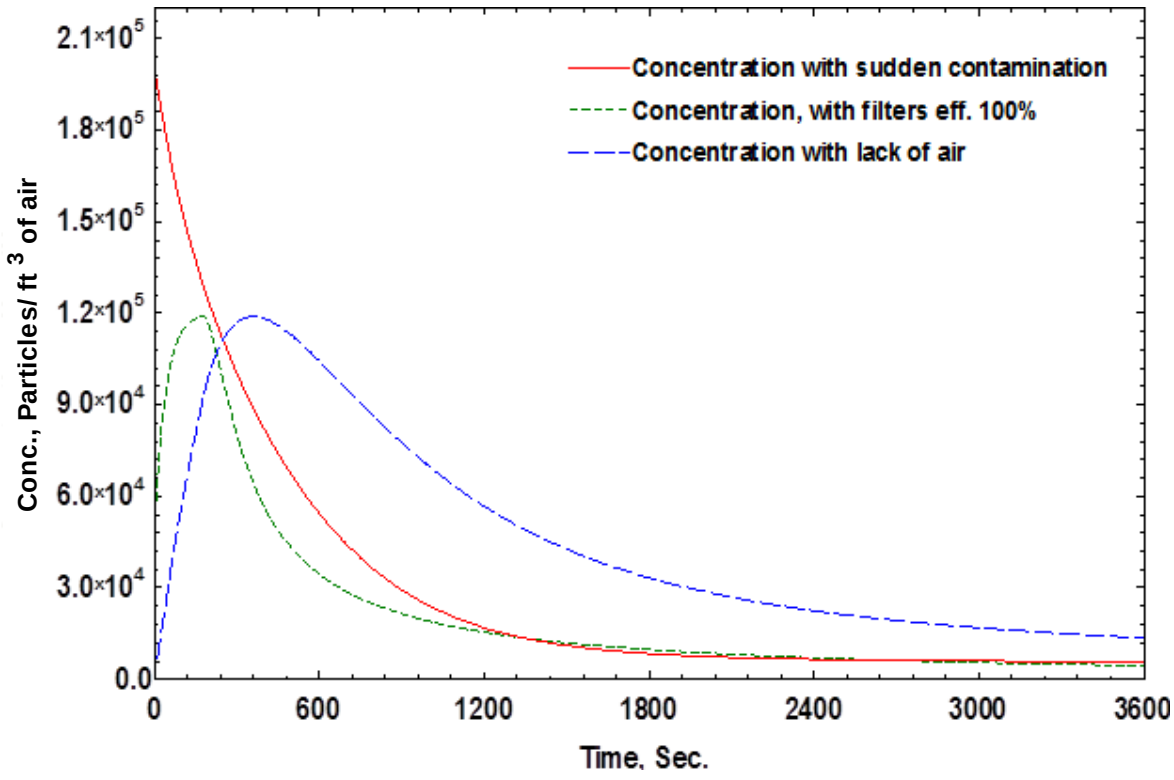

Fig. (4): Concentration with sudden contamination, 0.5 µm particle diameter

Dynamic analysis of clean room is illustrated and the results are differed according to clean area classification. The measured of particles' diameter is greater than 0.5 µm are illustrated in Fig. 3. The area is classified as class C according to ISO standard which have limit up to 353000 particles per cubic meter or 10,000 particles.ft^{-3}. Fig. 4 shows the concentration with sudden contamination, 0.5 µm particle diameter as well as shortage of supply air which means that the ventilation will last long time to clean the area.

The particles concentration results are calculated numerically applying finite difference scheme using equations 5 and 6. Initial count value is considered 5.0E6 particles and diameter 0.5 micron. The ventilation system particles balance relations are deemed as in Fig. 1 while the system is operated for approximately 30 min to achieve its function and removes contaminants until the area realizes the class counts. Fig. 3 shows logarithmic curve illustrates particles concentration variation with time while the ventilation system is running trying to expel the contaminants outside the room by using dedicated filters in the system entrance and sufficient very high efficiency filters in the entrance of clean room.

Fig 3 shows that time consumption for the normal system to clean the area from contaminants in startup (30 min) while it consumes more time in case of partial filter blocking (more than 60 min.)

Fig. 4 illustrates prediction in case of sudden contamination due to operation error and increasing contaminants to 1.95E+5 particles.ft^3 which shows that the system can expel the contaminants outside in 30 min, while it consumes more time in case of lack of supplied air to area.

5.1 Biological and particle Examination

This test is performed using special plates for this type of test. Perti plates are used and allocated in certain positions illustrated in positions as shown in the area layout in Fig. 2.

Table (2): The recommended limits for microbial contamination according to classified clean area in WHO technical report series 957 [9] are:

Class	Air Sample CFU/m^3	Settle plates Dia. 90mm, cfu/4hours	Contact plates Dia. 55mm, cfu/plate
A	< 1	< 1	< 1
B	5	5	5
C	50	50	25
D	100	100	50

Biological test is achieved using Perti plates with diameter 90 mm and coated with suitable two types of growth media:

1-Tryptic Soy Agar (TSA)

2-Dextrous Agar (DA)

The test is done after plates allocated in multiple positions as shown in Fig.2 for class A, and C.

Table (3): illustrate result of a batch during Tc^{99} production

Plate no	Position Class	DA media count, cfu	TSA media count, cfu
P_1	C	3	4
P_2	C	1	1
P_3	A	0	0
P_4	A	0	0

The number of Colony forming unit (cfu) is observed on a growth dedicated media after a growth time equals 15 days for microorganisms, which is the standard period dedicated for the test.

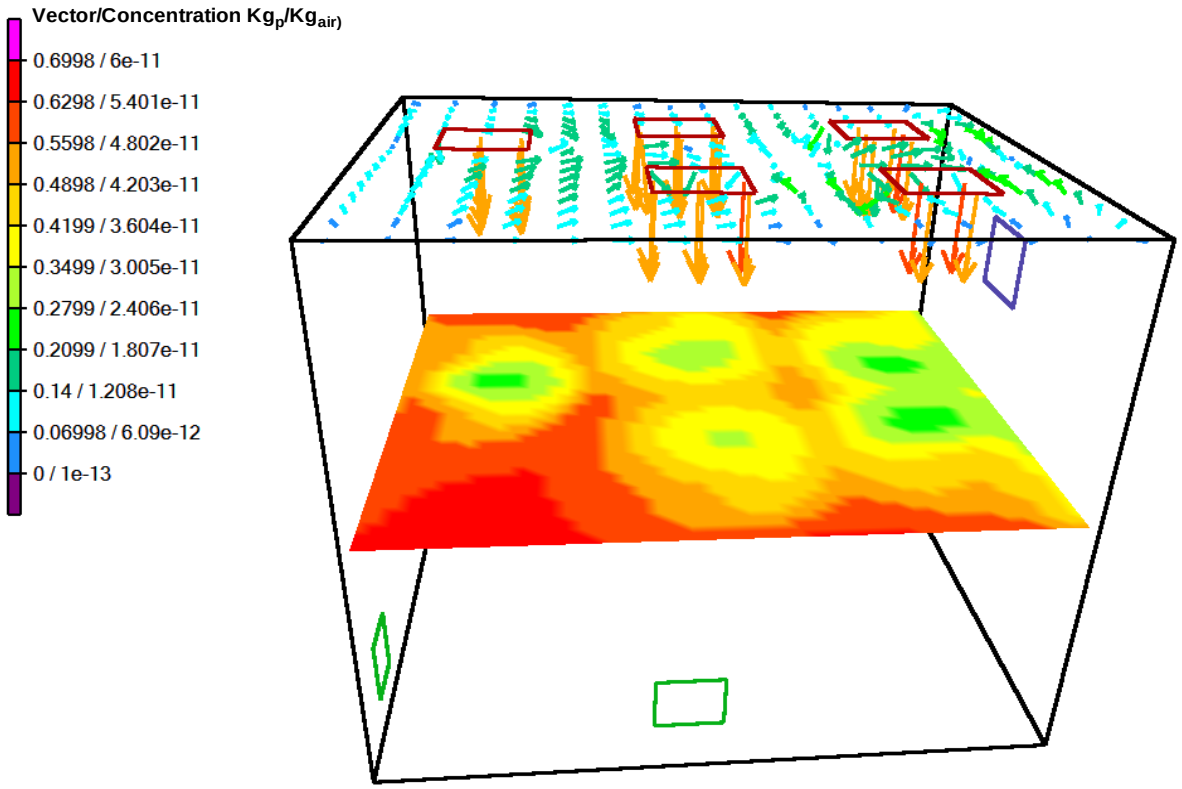

Fig. (5): CFD Particles concentration during startup ventilation

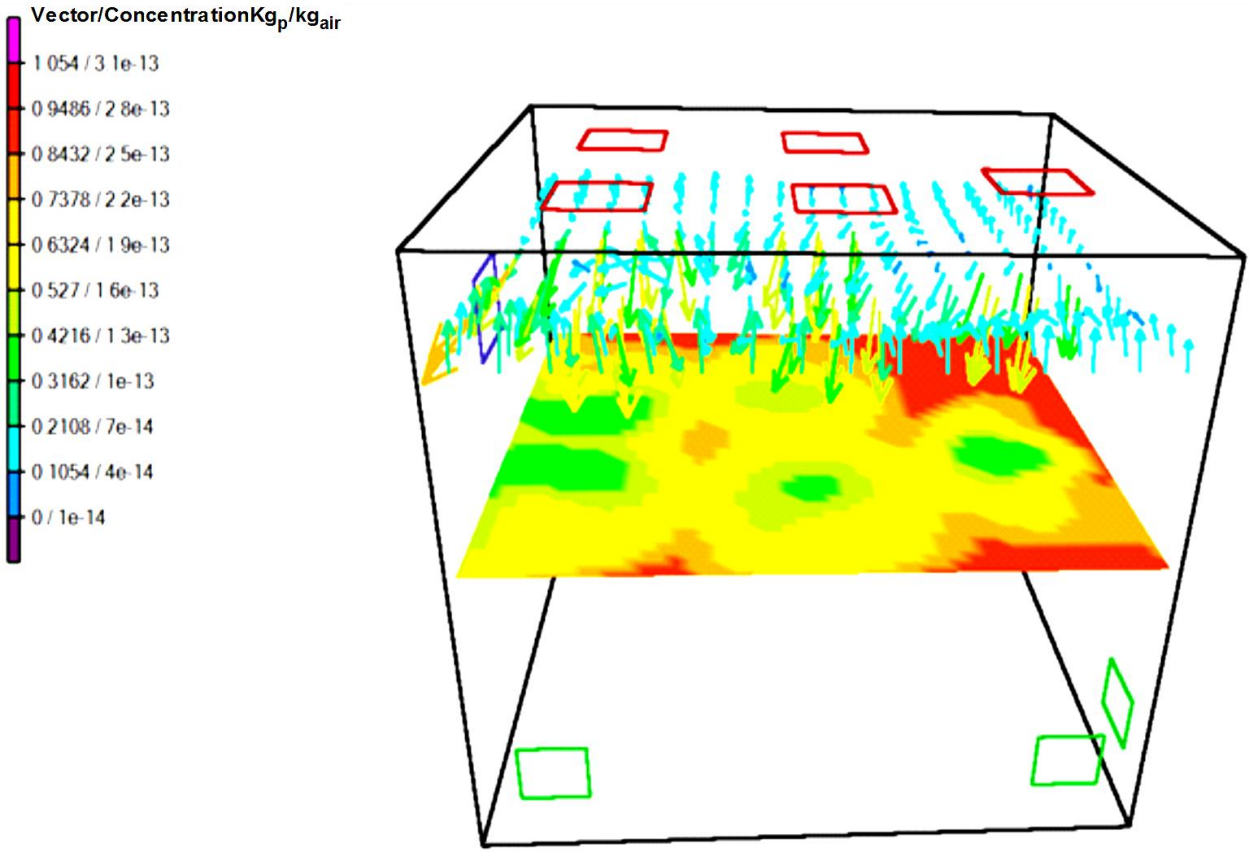

Fig. (6): CFD Particles concentration after steady state

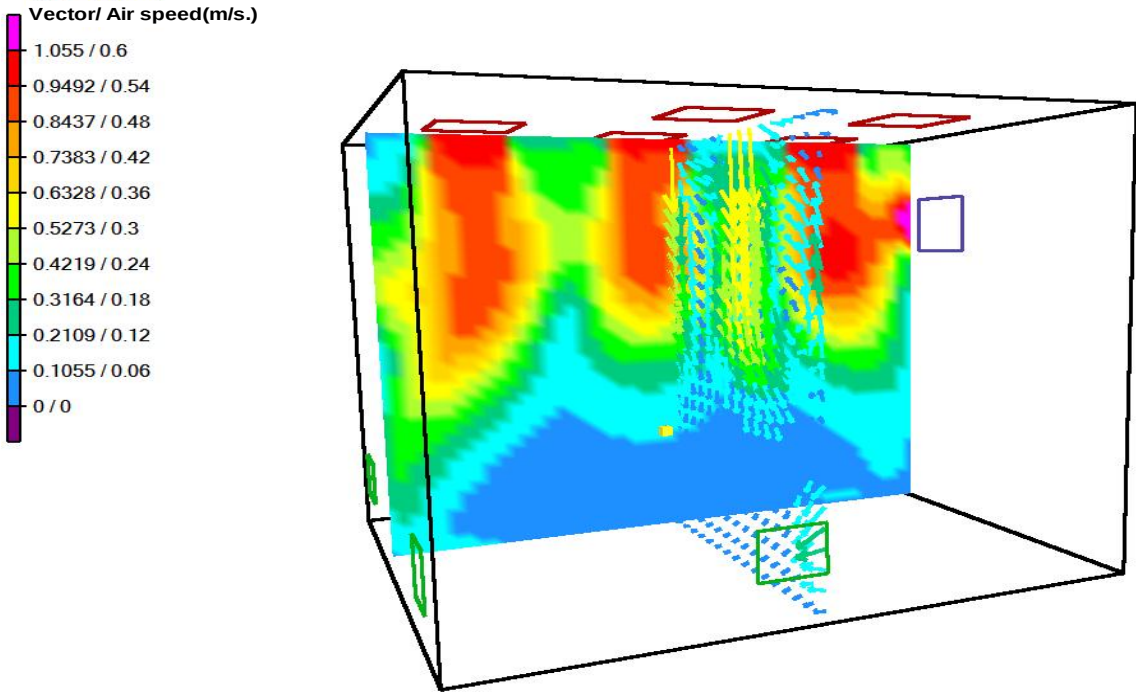

Fig. (7): CFD velocity distribution in the middle of clean room

Figs. 5, 6 and 7 illustrate CFD prediction of particle concentration in kg particles/kg air in both cases before and after running dedicated ventilation system as well as velocity distribution. The impact is illustrated clearly and the particles concentrations are changed and developed by ventilation system to realize the area class requirements to reduce the values from range (6E-12 to 6E-11) to become (1E-14 to 3.1E-13) which assumed acceptable within WHO standard. Fig 7 depicts CFD velocity distribution with arrowed streamlines as maximum air speed appears directly after the air outlets directly on the false ceiling is approximately 0.6 m. s^{-1} and streamline normally expels downstream to be extracted from bottom grills.

Particle counts are measured by EPC Ergotouch ET-01 airborne particle counter and shown in Fig. 8.

Fig. (8): EPC Ergotouch airborne particle counter

The equations below illustrate how the calculation can be conducted according to ISO standard no. 14644.

$$V_s = \frac{20}{C_n} * 1000$$

$$C_n = \left[\frac{0.1}{0.5}\right]^{2.08} * (10)^4$$

$$\bar{X} = \frac{X_1 + X_2 + X_3 + X_4}{n}$$

$$\bar{\bar{X}} = \frac{\bar{X}_1 + \bar{X}_2 + \bar{X}_3 + \bar{X}_4}{m}$$

$$SD = \sqrt{S^2}$$

$$UCL\_95\% = \bar{\bar{X}} + t_{0.95}\left(\frac{s}{\sqrt{m}}\right)$$

Where,

$\bar{X}_i$ is mean particle value at location i,

X_i is the reading in position i,

$\bar{\bar{X}}$ is the overall mean of the location averages.

n is number of readings in one position,

m is no of positions,

SD is standard deviation, and

S is variance

$t_{0,95}$ represents the 95th percentile (quantile) of the t distribution, with (m–1) degrees of freedom

UCL_95% is the upper confidence limit (UCL) for the overall mean

Position no.	Reading 1	Reading 2	Reading 3	Reading 4	$\bar{X}_i$
Position (P1)	1288	1362	1187	1124	1240
Position (P2)	888	930	962	865	912
Position (P3)	1189	810	917	870	947
Position (P4)	260	254	251	246	253
$\bar{\bar{X}}$					838

Time of sample= 10 min.

SD=128

No. of measurements per location=4

V_s=56.87.

UCL_95%=1131 [particles.ft^{-3}]

According to EU GMP classifications, the class C states that the calculated particle counts UCL_95% should not exceed 10,000 particles /ft^{3} and the value of UCL_95 is 1131 which is considered within the accepted value of the test.

CONCLUSION

The study deals with clean area simulation and analysis based on two criteria, the first is measuring and predicting the particle counts and evaluated it with area classification as well as the necessary time which is calculated for the dedicated ventilation system to achieve the removal of contaminants. In case of full filter efficiency the time is 35 min., while it lasts more than 60 min. to satisfy the level in case of 70% filter efficiency. Concentration with sudden contamination due to regulation break from operators is predicted and shows that ventilation system can purge area in 35 min., while with lack of supplied air the time for cleaning extends to more than hour. Concentration and velocity contour plots from CFD are illustrated also during startup till steady state and found 6E-11 kg particles/kg air, 0.7 ms^{-1} and 3.1E-13 kg particle/kg air, 1.054 ms^{-1}. The biological test as well estimates the number of colony forming unit (cfu) based on growth media and growth time required for microorganisms with 3 and 4 cfu when using different categories of perti plates for class C satisfying the limits. The ISO test is performed also illustrated the value of UCL95, which calculated and found 1131 particles.ft^{-3} particles and satisfies also standard limit of class C below 10,000 particles.ft^{-3}. The results show that the assigned airflow system is able to purge out internally generated particles effectively and there is good agreement between predicted and measured particle counts in dedicated area class in addition to good agreement with biological test results. An agreement also is noticed for particle counts in class area C under study with standard WHO series 957.

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