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Risk for contamination in a cleanroom with weakened aerodynamic barrier

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Abstract. The risk for contamination in a pharmaceutical cleanroom was investigated through tracer gas measurements in 13 different scenarios, when the aerodynamic barrier between an airlock (AL) and a cleanroom (CR) was weakened by opening the door separating the rooms. Air velocities through the doorway, differential temperature between the airlock and the cleanroom, different door opening speeds and different walking paces of a mannequin entering the cleanroom were the four parameters in focus. The study was conducted in a full-scale cleanroom mock-up (4.7 x 3.5 x 2.5 m), where each scenario was repeated three times. The results of the investigation show that air velocity through the doorway is the most important design parameter to ensure the aerodynamic barrier, when an average air velocity between 0.14 m/s (resulted in 209 l of migrated air) and 0.33 m/s (resulted in 62 l of migrated air), which was achieved at isothermal conditions and with a door opening time of 10 seconds. Increasing the door opening time to 20 seconds diminishes the effect of a higher air velocity to negligible levels. Last by not least, the differential temperature between airlock and cleanroom has an impact on the air migration, where a warm cleanroom (24 °C) and a cold airlock (20 °C) showed a low contamination risk with a door opening time of 10 seconds. A warm cleanroom (24 °C) and a cold airlock (20 °C) showed on the other hand a high level of air migration with almost 1.500 l of contaminated air entering the clean zone with a door opening of time 10 seconds.

1. Introduction
In the pharmaceutical production industry, controlled environments are used a mean to secure the medicine against contamination. Contaminated drugs present a great financial risk for companies and severe consequences for consumers such as the “Heparin Disaster” in 2008 turned out to be, where 81 people died from contaminated medicine due to allergic reactions [1]. As a result, the company that produced half of the Heparin medicine in America at that time had to revoke their products.

An aseptic controlled environment, where medicine production takes place, consists usually of a cleanroom with one or more adjacent airlocks. The barrier is secured by an overpressure in the cleanroom of e.g. 10-20 Pa [2-3]. The cleanliness in the cleanroom is obtained by highly-efficient-particles-air filters and high ventilation rates. However, when the door between cleanroom and airlock is being opened, the overpressure ceases to exist, and the aerodynamic barrier is as a result weakened. To secure a cleanroom against contamination, the current guidelines from FDA and EU offer design criteria concerning the design of the facility such as differential overpressure between a cleanroom and an airlock and minimum air changes [2-3]. However, information regarding the contamination risk in dynamic stances in a cleanroom are limited compared to the information for contamination risk under steady state, and the purpose of the current study was therefore to identify the most important parameters for creating and maintaining an aerodynamic barrier in a doorway under dynamic conditions.

Research regarding the minimum required air velocity through the doorway for securing the barrier has been conducted intensively by Ljungqvist and Reinmuller and Whyte and Farquharson respectively.
Their research shows that the minimum flowrate through a single hinged door is around 0.1 – 0.2 m³/s for maintaining the aerodynamic barrier under isothermal conditions [4-5]. However, in scenarios with a differential temperature between cleanroom and airlock of up to 4°C the required flowrate to maintain the barrier would increase to 0.3 – 0.9 m³/s [4-7]. A study by Yamaguchi et al demonstrated however that barrier to prevent air migration from airlock to cleanroom under isothermal conditions can be achieved with only 0.04 m/s corresponding to 0.1 m³/s for a single hinged door [8]. In another study, the contamination risk between a hinged and a sliding door was investigated, where the hinged door resulted in three times as much air migration towards the clean area compared to the hinged door [9-10]. The impact of door motions has furthermore been researched through CFD simulations and experiments, where it was demonstrated that the velocity magnitude caused by the opening of the door would be 0.1 m/s depending on the rotation speed of the door [11]. Similar studies show that the vortex of air entering the clean area created by a single hinged door can be reduced up to 6 times by switching to a sliding door [12-13]. Lastly, the impact on air migration caused by human movement has been studied at a hospital with sliding doors in the critical areas by Vilafruela et al [14]. The study shows that approximately 1.5 m³ air migrates to the clean area during isothermal conditions and with no differential flowrate between cleanroom and airlock.

2. Method
The study was carried out in a mock-up consisting of a cleanroom (CR) and an airlock (AL) as shown in figure 1. Set-up of the mock-up is described by Hashimoto et al who conducted similar experiments but with particles instead of tracer gas [15]. The cleanroom was supplied with filtered air, which was transferred to the airlock through two bypasses in the ceiling with small located fans in the airlock to mix the air. The cleanroom and the airlock had an area of 4.6 m² and 3.4 m² respectively with a room height of 2.5 m. The single hinged door between the rooms measured 2.05 m in height and 0.90 m in width. Passage through the door was simulated with a non-thermal mannequin attached on a movable board with a remote control. The mannequin had a surface area of approximately 1.8 m². Measurement of the tracer gas concentrations were performed with a Photoacoustic multi gas monitor at two location (Brüel&Kjær) with an accuracy of ± 2.5 % and an interval between each sampling channel of 30 sec. Additionally, a fast gas monitor with an accuracy of ± 50.0 % for low concentrations able to measure for each second was used [16]. The air velocity and the temperature in the doorway was measured by an omnidirectional anemometer with four multipoint sensors (Swema) with an accuracy of ± 0.03 m/s and ± 0.50 °C. The experiments consisted of three stages. First, air velocity measurements in the doorway under isothermal conditions for all four flowrate scenarios were conducted. Afterwards, smoke visualizations were performed. Finally, tracer gas measurements took place based on the collected data in the previous stages. The time setting for the experiments are shown in table 1.

![Figure 1. Known and unknown flowrates for scenarios 1-2 and plans below and above ceiling.](image-url)
Table 1. Time settings for the experiments.

| Procedure                  | Wait  | Open door | Wait  | Move mannequin | Close door | Total time |
|----------------------------|-------|-----------|-------|----------------|------------|------------|
| Slow door                  | 10    | 20        | 10    | No movement    | 5          | 45 sec.    |
| Fast door                  | 10    | 10        | 10    | No movement    | 5          | 35 sec.    |
| Slow door + mannequin      | 10    | 20        | 7     | 3              | 5          | 45 sec.    |

In the current investigation the risk of contamination was expressed as the air (tracer gas) entering the cleanroom from the airlock. The volume of air was equal to mass over concentration as seen in eq. (1).

\[ m = p_0 \cdot V \leftrightarrow V = \frac{m}{p_0} \]  

Where \( m \) [mg] was the total mass of the tracer gas migrating from the airlock to the cleanroom, \( p_0 \) [mg/l] was the initial concentration of the tracer gas in the airlock and \( V \) was the volume [l] migrating across the door. The initial concentration \( p_0 \) would remain constant during the experiments. The total amount of tracer gas was then calculated by integrating the exhaust concentration over time as seen in eq. (2).

\[ m = Q \cdot \int_0^\infty p(t) \, dt \]  

Where \( Q \) was the total exhaust flow rate [l/s] and \( p(t) \) [mg/l] was the measured tracer gas concentration in the exhaust. Substituting eq. 2 with eq. 1 the total volume exchange across the doorway induced by the door operation was expressed on a form as seen in eq. (3).

\[ V = Q \cdot \int_0^\infty \frac{p(t)}{p_0} \, dt \approx Q \cdot \sum_i \frac{p_i}{p_0} \Delta t_i \]  

Where \( p_0 \) [mg/l] was the initial tracer gas measurement in the airlock, \( p_i \) [mg/l] was the ith measurement after the door operation and \( \Delta t_i \) [s] was the sampling period of the ith measurement. One experiment consisted of three door openings, each separated by 10-20 minutes to create a steady state condition in the airlock. To simulate the decay time the decay method for gasses shown in eq. (4) were used.

\[ C(t) = C_0 \cdot e^{-nt} \]  

Where \( C_0 \) [ppm] is the initial concentration in the cleanroom, \( n \) (h\(^{-1}\)) is the air exchange, while \( t \) (s) is the time. The invasion ratio was expressed as the volume of migrated air divided by the volume of air in the airlock as shown in eq. (5).

\[ IR = \frac{V_{migrated \, air}}{V_{airlock}} \]  

The average air velocity was found by measuring the velocity at 10 locations forming a cross in a 3 x 6 grid in the doorway with the door open all the time. The smoke visualizations were made with smoke generated in the airlock and laser sheets mounted horizontally and vertically inside the cleanroom.

3. Results

The smoke visualizations are illustrated in figure 2–3, where figure 2 shows vertical views towards the cleanroom with a door opening time of 20 seconds without a mannequin entering the cleanroom and with a mannequin moving 1.0 m/s into the cleanroom. The figure shows both the air disturbances the movement of the mannequin causes, and the air migration from the door opening operation, which can be seen after 5 seconds. The flowrate through the door in figure 3 with horizontal views was in both cases set to 110 l/s with the door opening speed as the only variable parameter. It is observed for a fast door opening operation that air is entering the room after 5 seconds, where nothing or very little is seen for a slow door opening operation.
The tracer gas results displayed in table 2 shows the risk of contamination expressed as air migration in litres from airlock to cleanroom for the three repetitive experiments for each scenario. The conditions for each scenario are shown in the table as well.

Scenarios 1-7 concerned isothermal conditions with different flowrates and door opening speeds, while scenarios 8-9 investigated the movement of the mannequin, hence with a fast pace of 1.0 m/s and a slow pace of 0.5 m/s. The differential temperature between cleanroom and airlock were investigated in scenarios 10-13. The parameters of investigation such as walking pace, door opening time, air velocity in the doorway and differential temperature between cleanroom and airlock is furthermore illustrated in figure 4, where each graph in the figure shows the contamination risk displayed as migrated air in litres as a function of the mentioned parameters.

Figure 2. Vertical visualizations – door opening (slow) and movement of the mannequin (fast).

Figure 3. Horizontal visualizations – fast door opening (10 sec.) and slow door opening (20 sec.).
Table 2. Conducted tracer gas scenarios with migrated air from airlock (AL) to cleanroom (CR).

| Scenario | Flowrate through the door [l/s] | Q/A * [m/s] | Opening time [s] | Average v through the door [m/s] | Air changes in CR [h⁻¹] | ΔT [°C] | Pace [m/s] | Migrated air [l] | Standard deviation [l] | Invasion ratio [%] |
|----------|---------------------------------|-------------|-----------------|-------------------------------|-----------------------|--------|------------|-----------------|----------------------|-------------------|
| 1        | 110                             | 0.06        | 10              | 0.14                          | 30                    | 0      |            | N/A             | 209                  | 31.5              | 2.9          |
| 2        | 110                             | 0.06        | 20              | 0.14                          | 30                    | 0      |            | N/A             | 54                   | 4.7               | 0.8          |
| 3        | 170                             | 0.08        | 10              | 0.15                          | 45                    | 0      |            | N/A             | 225                  | 11.4              | 3.1          |
| 4        | 170                             | 0.08        | 20              | 0.15                          | 45                    | 0      |            | N/A             | 82                   | 2.0               | 1.1          |
| 5        | 335                             | 0.17        | 10              | 0.23                          | 90                    | 0      |            | N/A             | 105                  | 9.2               | 1.5          |
| 6        | 335                             | 0.17        | 20              | 0.23                          | 90                    | 0      |            | N/A             | 45                   | 7.3               | 0.6          |
| 7        | 460                             | 0.23        | 10              | 0.33                          | 125                   | 0      |            | N/A             | 62                   | 12.6              | 0.9          |
| 8        | 335                             | 0.17        | 20              | 0.23                          | 90                    | 0      |            | 1.0             | 122                  | 13.7              | 1.7          |
| 9        | 335                             | 0.17        | 20              | 0.23                          | 90                    | 0      |            | 0.5             | 62                   | 6.8               | 0.9          |
| 10       | 335                             | 0.17        | 10              | 0.23                          | 90                    | 4 **   | N/A        | 1484            | 37.2                 | 20.5              |
| 11       | 335                             | 0.17        | 20              | 0.23                          | 90                    | 4 **   | N/A        | 120             | 6.7                  | 1.7               |
| 12       | 335                             | 0.17        | 10              | 0.23                          | 90                    | 4 ***  | N/A        | 40              | 5.7                  | 0.6               |
| 13       | 335                             | 0.17        | 20              | 0.23                          | 90                    | 4 ***  | N/A        | 25              | 4.0                  | 0.4               |

* Flowrate through door divided by area of the door
** Scenarios 10-11 with $T_{cleanroom}$ of 20 °C and $T_{airlock}$ of 24 °C (warm airlock)
*** Scenarios 12-13 with $T_{cleanroom}$ of 24 °C and $T_{airlock}$ of 20 °C (cold airlock)

It is seen in figure 4 that increasing the walking pace from 0.5 m/s to 1.0 m/s increases the air migration with 100 %. The difference between a slow and a fast door opening is also highlighted in the same figure, where large differences is shown with a flowrate of 110 l/s through the door with a fast and a slow door opening time. When the flowrate is increased to 460 l/s the effect of opening the door slow versus fast is neglected however. The differential temperature between cleanroom and airlock shows a significant difference between a cold cleanroom versus a warm airlock and a warm cleanroom versus a cold airlock.

4. Discussion

The results in table 2 and figure 4 shows a clear difference between high and low flowrates, high and low walking paces and fast and slow door opening times as means to secure the aerodynamic barrier. It was also demonstrated that an airlock with lower air temperature had the lowest contamination risk compared to a case, when the airlock had a higher air temperature than the cleanroom. This may have been caused by higher air velocities at the bottom than the top of the doorway suggesting that the air
transfer happened as displacement ventilation. Uncertainties in the results must also be expected regarding the steady state conditions in the airlock, which depended on the location of the fans and the dosing points. Additionally, the time settings for the experiments may have caused irregularities in the gas concentration in the airlock, which would have had an impact on the concentration in the cleanroom. This is seen in scenarios 1-4, where it is shown that a flowrate through the door of 110 l/s leads to a smaller migration than 170 l/s.

5. Conclusion
Amongst the different parameters of interest air velocity and door opening speed was identified as the most important parameters for maintaining the aerodynamic barrier. The parameter walking pace also had a significant impact, where it was shown that moving with 1.0 m/s instead of 0.5 m/s increased the contamination risk by 100 %. Lastly, non-isothermal scenarios showed hence a large and a small contamination risk depending on whether the airlock was warm or cold. The results related to the non-isothermal conditions need validation though, before a conclusion can be made. Although it is tempting to say that future design principles for cleanrooms and airlocks needs to focus more on different temperature sets between the two rooms.

References
[1] Naydenov K 2016 Resume of research project agreement between Ramboll and The Technical University of Denmark
[2] EN ISO 14644-1 2015 Cleanrooms and associated controlled environments – Part 1 Classification of air cleanliness by particle concentration
[3] EN ISO 14644-4 2001 Cleanrooms and associated controlled environments – Part 4 Design, construction and start-up
[4] Ljungqvist B and Reimuller B 2002 Clean room design – Minimizing contamination through proper design INTERPHARM/CRC
[5] Ljungqvist B, Reimuller B, Gustén J and Nordenadler J Dispersion of airborne contaminants through door openings in operating room – Some calculations
[6] Whyte W 2001 Cleanroom technology – Fundamentals of design, testing and operation JOHN WILEY & SONS
[7] Whyte W 1999 Cleanroom design JOHN WILEY & SONS
[8] Yamaguchi T, Kondo A and Kaga A 2015 Study on doorway airflow for maintaining clean environment
[9] Kalliomäki P, Saarinen P, Tang J and Koskela H 2016 Airflow patterns through single hinged and sliding doors in hospital isolation rooms – Effect of ventilation, flow differential and passage Building and Environment 107, 154-156
[10] Saarinen P, Kalliomäki P, Tang J and Koskela H 2015 Large eddy simulation of air escape through a hospital isolation room single hinged doorway – Validation by using tracer gases and simulated smoke videos
[11] Hathway A and Papakonstantis 2015 CFD simulation of airflow due door motion using a momentum source method IBPSA Vol. 14 India
[12] Fontana L and Quintino A 2014 Experimental analysis of the transport of airborne contaminants between adjacent rooms at different pressure due to the door opening Building and Environment 81, 81-91
[13] Lee S, Park B and Kurabuchi T 2016 Numerical evaluation of influence of door opening on interzonal air exchange Building and Environment 102, 230-242
[14] Vilafruela J, San Jose J, Castro F and Zarzuelo A 2016 Airflow patterns through a sliding door during and foot traffic in operating rooms Building and Environment 109, 190-198
[15] Hashimoto K, Shao X, Fang L and Melikov A 2018 Experimental assessment of airborne transmission using particles during the door behavior
[16] Kierat W and Popiolek Z 2016 Method of the gas concentration sinusoidal and step changes generation for dynamic properties of gas concentration meters testing Building and Environment 88, 131-136