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Experimental investigation into cleanroom contamination build-up when applying reduced ventilation and pressure hierarchy conditions as part of demand controlled filtration

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\textbf{Abstract}

The use of cleanrooms is increasing and the expectation is that this growth will continue in the coming decade. When compared to an average office building, cleanrooms consume large amounts of energy due to their high Air Change Rates (ACRs) and strict air conditioning requirements. Application of Demand Controlled Filtration (DCF) is a means to reduce the (fan) energy demand. The question is whether the air quality is compromised at reduced ACR and overpressure conditions in the non-operational hours of a cleanroom. In a cleanroom mock-up, experiments have been performed to investigate the particle concentration build-up for different cases with DCF, including an extreme case with zero ACR and zero pressure difference. For the DCF conditions and the specific case study, conditions for particle concentration outside the cleanroom, that may still provide high-quality Good Manufacturing Practices (GMP) conditions in the cleanroom, are derived from the results. Furthermore, it assumes DCF application via occupancy sensing, i.e. starting DCF 30 min after the last person left the cleanroom. When applying DCF for a normal workweek (production 08:00–17:00), fan energy savings higher than 70\% can be obtained without compromising the air quality requirements under normal circumstances. DCF, in combination with a reduced pressure difference, therefore is regarded as a feasible solution to reduce the energy demand of cleanrooms when the personnel in the cleanroom are the main source of contamination. These results are obtained for the presented case study. Though assuming a conservative approach, confirmation of these outcomes for other cleanrooms is recommended.

\textbf{1. Introduction}

Cleanrooms and controlled environments are widely applied in many industries. Their prospective global market size Compound Annual Growth Rate is 5.1\%, until at least 2025 [1]. Cleanrooms are energy-intensive facilities. Pharmaceutical cleanroom facilities consume up to 25 times more energy than an average commercial building. 50–75\% of the electrical energy demand in these facilities is from the heating, ventilation and air conditioning (HVAC) system. The main reason for the high energy consumption is their high Air Change Rate (ACR) that guarantees the air quality required by these spaces [2].

Two ventilation methods are commonly used to control the airborne contamination level: Displacement of particles by a unidirectional airflow (UDAF) or dilution of particles by a non-UDAF. The latter is often used for pharmaceutical cleanrooms or cleanrooms with ISO class 6 and less clean areas [3]. The air quality in pharmaceutical cleanrooms is based on ISO 14644-1 and GMP (Good Manufacturing Practice) classification guides [3,4]. These guidelines classify cleanrooms based on the acceptable number of airborne particles and Colony Forming Units (CFUs) per m\(^2\) of air. The GMP has four classes and makes a distinction between a room “in use” (occupied, operational) or “at rest” (non-occupied, non-operational). In fact, people are (in many cases) the biggest source of pollution and therefore disturb the particle equilibrium when they enter the room [5].

Energy efficiency of a cleanroom facility, including its HVAC system, up till now, has been given less weight in the design, when compared to the reliability and yield of the production process [6]. During the design process, the particle generation rate is often not known [7]. Therefore,
designers generally use prescribed values for airflow rates from the International Society of Pharmaceutical Engineering [8]. This approach increases the risk of the design being oversized. Oversized systems will ensure that indoor air quality requirements are met; but, it will also unnecessarily increase the energy demand for operating the fan, in combination with the required pressure hierarchy, and the extra air conditioning [9–11].

With the Paris agreement on climate change [12], EU member states have the obligation to reduce greenhouse gas emissions by 40% by 2030, compared to 1990 levels [13]. Industry, including cleanroom facilities and related spaces, therefore face the challenge to become more sustainable to meet the legal goals. The recently released ISO 14644-16 provides recommendations for energy-saving methods and optimization techniques at each stage in the cleanroom life cycle [14].

It is common for GMP classified spaces to run the Air Handling Unit (AHU) 24 h a day, 7 days a week, even during the non-operational hours. Simple handling modifications, such as lowering the airflow in these periods, can result in energy-savings without excessive particle concentrations in the cleanroom [15,16]. ISO 14644-16 recommends to turn-down or even turn off airflow during non-operational hours. It will not only save energy, but also air conditioning energy. GMP annex 1 [14], and its currently available draft version [17], nevertheless, still highly recommend to maintain a pressure hierarchy under all operational conditions. A previous experimental study showed potential fan energy-savings up to 93.6% by implementing DCF. That study recommended to apply this control strategy based on occupation and not on particle concentration [18]. Therefore, only a distinction needs to be made between operational and non-operational conditions. Another study showed a 70–75% energy reduction of the recirculation AHU by turning down the make-up air unit 30 min after the last occupant leaves the cleanroom [19,20]. Literature does not provide a typical flow reduction rate during these non-occupied periods. The number varies between 25 and 50% [16,21] to 70% [22] of the total volume flow rate. In addition, scientific literature (Web-of-Science, Elsevier ScienceDirect; search string ‘cleanroom AND ventilation’; last five year; Research articles) does not show recent research outcomes related to the particle concentration in DCF mode during non-operational hours. Only [16] provides such information, but with limited context.

Changing the ACR in non-operational hours may result in certain risks with respect to the particle concentration [14]. Physical barriers, such as pressure hierarchy, prevent the ingress of particle contamination from lower or non-classified spaces into the cleanroom. Reducing the pressure difference between rooms reduces the protection grade [23]. Another risk is that the cleanroom must be able to restore back to the required cleanliness conditions during restart of the system, within a certain recovery time. A final potential risk is the accessibility of the cleanroom entry points. These should be closed during the non-operational hours until the system is fully operational again to prevent excessive particle contamination in the cleanroom. Therefore, extra steps must be taken during the commissioning and validation of cleanrooms with DCF [16].

The work from Loomans et al. [18] identified the (fan) energy savings possible from applying DCF for the investigated pharmaceutical cleanrooms. In that work, it was assumed that the air quality and contamination was not affected by the reduced flow rates and pressure hierarchy. This assumption, however, was not investigated and literature does not provide clear support for it at reduction rates >70%. In order to determine the potential of DCF further, the objective of this research, therefore, is to assess to what extent a reduced flow rate and pressure hierarchy affect the air quality in a cleanroom. The research question to be answered is whether a reduced flow rate and/or a reduced pressure hierarchy affect the air quality such that its application in practice would not be advocated. The study focuses on the applicability of ACR and pressure hierarchy reduction in non-operational hours.

2. Method

To answer the research question, an experimental approach was taken. An experimental mock-up was used to investigate a number of cases in which the airflow rate was reduced, in combination with a reduction in the pressure hierarchy.

2.1. Location description

The cleanroom mock-up (3.0 m × 2.4 m × 3.0 m [LxWxH]) applied was located in an assembly hall for cleanroom walls, as shown in Fig. 1. The cleanroom was exposed to the hall conditions on all its sides, with the exception of the floor. A sealed tarpaulin tent was placed in front of the entrance to protect the cleanroom against activities in the hall (tent not shown in Fig. 1). The cleanroom occupancy state was “as-built” [3]. A voltage controllable box fan (Systemair KVK slim 250) was placed between the supply and return duct to generate the desired airflow rate and pressure hierarchy in the cleanroom (Fig. 2). Air flows through a Constant Air Volume (CAV) control valve (Trox RN160) towards the HEPA filter (H14 filter class) and via a swirl diffuser directly into the cleanroom. The swirl diffuser establishes a non-UDAF ventilation pattern in the cleanroom. The measured particle concentration at the supply grill is zero when the cleanroom is operational. The CAV valve in the return duct was used to tune the overpressure in the cleanroom for the different cases and conditions during the experiment. For that the pressure difference was measured continuously (at 1 min sample time) between the cleanroom and the adjacent space. A duct that supplies fresh pre-filtered air (filter class G4), containing a control valve (Trox AK120), was connected to the system to supply enough air into the system. The fan had a maximum volume flow rate of 1318 m³/h, which is equal to an ACR of 61 h⁻¹. The maximum delivered ACR in the cleanroom mock-up was 20 h⁻¹ (432 m³/h) due to the system’s static pressure. The mock-up had an air leakage class L1, which is based on the pressure and air tightness of the cleanroom [24].

The cleanroom floor and door were cleaned with appropriate, alcohol-based, cleaning materials at the start and end of every experiment, including the installed fan box and ducts. The arrows show the airflow direction. Tarpaulin tent in front of the cleanroom not shown on the picture.
measurement day. An anti-dust, sticky mat was placed in front of the entrance door and its sheets were replaced frequently.

2.2. Measurement equipment

The environment in and outside the cleanroom environment was monitored using several sensors. Table 1 summarizes them. In total, four light-scattering, airborne particle counters (PCs), that applied different flow rates, were used during the measurements. Their specifications are summarized in Table 2. Particle generation was represented through a flow series for one case. By treating the data relative to the particle concentration measured at PC1 (outside; at particle size level), the effect of this variation was taken into account. With this approach, it is also possible to generalize the outcomes to other situations.

All counters have a storage capacity of 100 samples. As the total experimental time may vary per case, the sample time varies per experiment. Though the (calibrated) particle counters were obtained from the manufacturer directly, a correction factor for the particle concentration, for each particle size investigated (≥0.3 μm, ≥0.5 μm, ≥1.0 μm, ≥3.0 μm and ≥5.0 μm), is obtained by measuring the particle concentration at the same single square meter with all four calibrated counters. The correction factor for each counter is taken into account when analyzing the data.

When the airflow velocity is lower due to reduced flow rates, large temperature variations may result in undesired airflow disturbances. Therefore, the temperature of the floor, wall, room, inlet, and outlet were monitored. Furthermore, airflow in the duct was measured with a micro-manometer and pitot tube before and after every measurement according to ISSO publication 31 [25]. The duct flow airspeed was measured to assure consistency of the desired ACR during an experiment. Fan energy use was monitored to determine the difference in energy use between the different cases investigated.

### Table 1

| Sensor | Type | Unit | Accuracy | Function |
|--------|------|------|----------|----------|
| Differential pressure | Dwyer | [Pa] | ±1 [%] | Measure the pressure difference between cleanroom and adjacent space. |
| | Magnesense | | | |
| Pitot tube and micro-manometer | ALNOR EBT720 | [m/s] | ±2.5 [%] | Measure duct airflow to calculate the supply and return air. |
| Temperature sensor 4x | – | [°C] | ±0.5 | Measure temperature in cleanroom at four described positions. |
| Energy meter | – | [pulses/ kWh] | – | Measures the number of pulses over time. 1000 pulses per hour is 1 kW h. |
| Data logger | Squirrel SQ20202 | [–] | – | Log Temperature, Differential pressure and fan energy. |

### Table 2

| Name | Particle counter | Flow rate [l/min] | Particle size [μm] | T and RH [%] | Accuracy [%] | Calibrated |
|------|----------------|------------------|-------------------|---------------|--------------|------------|
| PC 1 | Lighthouse 3016 | 2.83 | 0.3-0.5-1.0-3.0-5.0 | Yes | 5 | Yes |
| PC 2 | Lighthouse 3016 | 2.83 | 0.3-0.5-1.0-3.0-5.0 | Yes | 5 | Yes |
| PC 3 | MetOne 3400 | 28.3 | 0.3-0.5-1.0-3.0-5.0 | No | 5 | Yes |
| PC 4 | MetOne 6000 | 28.3 | 0.5-5.0 | No | 5 | Yes |

2.3. Measurement plan

Three different cases were investigated. The cases differ in airflow rate and pressure difference. They are summarized in Table 3. A distinction was made to assess the effect of a minimum flow rate and pressure difference as compared to the extreme case of no ACR and pressure difference.

Fig. 3 provides a summary of the complete experimental set-up. The goal was to replicate a realistic situation by applying DCF. For an experiment (case), this means that the cleanroom is fully functional at the start of the experiment (stage 1). For that, we controlled the cleanroom at an ACR of 20 h⁻¹ and a pressure difference of 125 Pa. In this period a (normal clothed) person, serving as a particle source, was present in the cleanroom. This assured that the particle concentration in the cleanroom was higher than the supply condition and was in line with a realistic situation. In line with the outcomes from Ref. [18] the set-up was run for 30 min at normal level after the particle source was removed. This would represent the personnel leaving the cleanroom. After the 30 min delay, the flow rate and pressure hierarchy were adapted in line with the cases investigated (stage 2). The experimental time was determined by the time required to obtain a (near) steady-state situation for the contaminant concentration in the cleanroom at the reduced flow rate and pressure difference conditions. For Case 1 this meant a total experimental time of nearly 17 h, whereas for Cases 2 and 3 an experimental time of 3 h and 45 min was required. At the end of the experiment, the set-up again was run in fully functional mode (stage 3). In this case, no source (person) was introduced in the cleanroom. Stage 3 was not always part of the recorded measurements. Each case was repeated at least once to assess its reproducibility.

Of the four particle counters (PCs) applied in the set-up, one PC (PC1) was always positioned outside the mock-up cleanroom. The other three counters (PC2-4) were positioned inside. Information on their position is provided in Fig. 3. They were positioned at 0.8 m height to represent the typical height of a desk (work bench). Particle concentration was recorded at sizes ≥0.3 μm, ≥0.5 μm, ≥1.0 μm, ≥3.0 μm and ≥5.0 μm. The outside contamination conditions could not be controlled. Therefore, differences in absolute particle concentration levels existed between the investigated cases and individual measurement series for one case. By treating the data relative to the particle concentration measured at PC1 (outside; at particle size level), the effect of this variation was taken into account. With this approach, it is also possible to generalize the outcomes to other situations.

2.4. Data processing

For the data analysis, not all 100 samples per measurement were
used. Fig. 4 provides examples of the particle concentration as measured for one measurement series, for Case 1. In the analysis, only data samples that refer to the (near) steady-state part of stage 2 of the experiment were applied. This means that only samples 60–89 are used. To filter out (short-term) variations that may arise, samples are averaged per 5 samples, see Fig. 4 results for 0.5 μm. As a result, per measurement series six data points are available (1 = 60–64; 2 = 65–69; 3 = 70–74; 4 = 75–79; 5 = 80–84; 6 = 85–89). Further analysis was performed for these data points. A similar approach was taken for the analysis of the measured temperatures. Note that the first sample numbers, as presented in the graphs in Fig. 4, show the performance of the cleanroom ‘in operation’ and the effect of the 30 min delay after the person has left the room.

All particle concentration data, as measured inside the mock-up, for the different sizes investigated, were calculated relative to the concentration outside according to Equation (1). Data was treated separately for the different particle sizes investigated and for each data point, individually:

\[
PC_{x} \#\mu m_{\text{datapoint}}^{\text{rel}} = \frac{PC_{x} \#\mu m_{\text{datapoint}}}{PC_{1} \#\mu m_{\text{datapoint}}} \tag{1}
\]

In Equation (1), PCx refers to the particle counter PC2-4 inside the cleanroom, #μm to the individual particle sizes investigated and datapoint# refers to the individual data point as derived for the average of 5 samples (for samples 60–89). The approach aligns with the Contaminant Ratio as defined by Ref. [26].

Normality of the data points (per measurement case, per particle counter, per particle size) was checked with the Shapiro-Wilk test [27].
Normality was not identified for each set of data points (W ranged between 0.47 and 0.99), either by rejecting the hypothesis of normality, or because, in case of accepting the hypothesis, the p-value was >0.05. As, in addition to that, the number of data points per analysis was limited to six, the assumption was that normality was not guaranteed. Therefore, the results were checked on reproducibility, applying the Wilcoxon signed-rank test (two-sided). Significance was assumed at p < 0.05. The same test was performed to identify similarity between the three particle counters (PC2-3/2-4/3-4) within the cleanroom for a measurement series. The analysis was performed using Matlab 2018b [28]. Reproducibility and similarity were not confirmed for any of the measurement series and its combinations, either because of rejection of the null hypothesis (samples with equal medians), or because of p > 0.05, in case the hypothesis was accepted. Therefore, for a case, differences in the relative particle concentration between measurement series and within the mock-up were possible. This may be due to the fact that, at reduced or zero ACR, mixing is less prominent than when the cleanroom is functioning in normal mode, at high ACR. As a result, a conservative approach was assumed by regarding the measurement outcomes from the individual counters as individual outcomes. These outcomes thus were regarded as individual data points for a case as described. This assumption assures the inclusion of more extreme results, as derived from the measurements, in the analysis. Boxplots have been applied to identify the variation in outcome. Further information on the outcomes is provided in the results section.

3. Results

Table 4 presents some examples of outcomes of the absolute particle concentration as measured for the different cases. Note that the particle concentration for the surrounding environment was not controlled and, therefore, differed between the different measurement series. All further data presented in this section, therefore, is made relative, according to Equation (1), in order to compare and combine the results.

Fig. 5 summarizes the relative concentration at the identified sample points (data points) as derived from the measurement series for Case 1 for the different particle sizes. The results show that the concentration in the cleanroom, for the Case 1 conditions – no ACR and no pressure hierarchy – is 20 times lower than the concentration outside the cleanroom for nearly all measurements. The relative concentration at the identified data points for Case 2 and Case 3 are presented in the Annex, Fig. A.1.

Fig. 6 summarizes the relative concentration as a function of the particle size for the three cases investigated. Here, all data points as measured for the individual measurement series per case have been combined to derive the boxplots. Quantitative data of the boxplot quantiles (2.5%, 25%, 50%, 75% and 97.5%) are summarized in the Annex, Table A.1.

Temperature gradients were derived from the measured air and surface temperatures. To determine the temperature difference between the air and floor and wall, the air temperature was determined from the average of the supply, exhaust and air temperature measured at PC2. The derived temperature gradients are summarized in Table 5. They present the maximum of the temperature difference that was analyzed from the data points, as obtained. Additionally, the maximum temperature difference between supply and air temperature measured at PC2 is presented in Table 5.

Finally, an estimation of the energy savings potential is summarized in Table 6. Fan power in full operational mode was 413 W. For the assessment of the energy demand for a production day, the assumption is made that the fan operates from 8:00-17:30 h, this includes the 30 min delay in fan reduction after the last person left the cleanroom. For the yearly analysis a 5-day workweek is assumed.

4. Discussion

4.1. Particle concentration

The results of the measurement series (Fig. 6) show that the particle concentration in the cleanroom was affected by the conditions outside the cleanroom when the ACR and pressure hierarchy were reduced. Effects were most noticeable when both were set to zero (Case 1). Nevertheless, even in that case, the concentration inside remains at a 20 times lower level than the outside conditions. A reduced but non-zero ACR (4 h⁻¹; Case 2), in combination with a reduced but non-zero pressure hierarchy (4 h⁻¹, 7.5 Pa overpressure; Case 3) can keep the concentration inside at near-zero levels, despite the high particle concentrations outside. Reductions in the order of 2000 and higher are obtained for those cases.

These outcomes show that it is possible to reduce the ventilation conditions in cleanrooms when non-operational. It does assume a ‘clean’ start of the non-production phase, in line with [19], by continuing the original flow conditions at least 30 min after the last occupant leaves the room. The results of the effect of a reduced ACR are in line with outcomes from Ref. [19], though the said work did not implement the more extreme conditions that were investigated in this work. The flow reduction we investigated is 80–100% while literature recommends reducing the flow by 25–50% [16,21] till 70% [22]. Our work shows that higher flow reductions do not compromise the cleanroom performance, whilst providing additional energy savings. It may be possible to apply other ventilation strategies, e.g. based on fuzzy logic [29] or particle concentration [18]. A reduced flow rate as a result from such a strategy would benefit from the results presented here, under the assumption that the cleanroom is clean at the start of the chosen ventilation strategy.

When translating the outcomes to minimum requirements for the particle concentration outside the cleanroom, this would lead to the results as presented in Table 7. It shows the maximum allowable particle concentration for the DCF conditions investigated when assuming the 97.5% quantile of the measurement outcomes for the individual cases as function of the EU GMP/ISO requirements [3,4].

Comparing the results from Table 7 to the measured absolute particle concentrations presented in Table 4, for the experimental conditions outside the cleanroom, it shows that for Case 3, GMP Class A conditions can still be obtained in the cleanroom. For Case 2, for particles≥5.0 μm, a Class C is achieved, while for particles≥0.5 μm, Class A is still obtained. For Case 1, only Class C and D can be obtained for particles≥0.5 μm. For Case 1, only Class C and D can be obtained for particles≥0.5 μm.
μm and ≥5.0 μm, respectively. It should, however, be noted that the experimental conditions outside the cleanroom were not typical for a normal cleanroom facility. Therefore, one may assume that higher Classes (at rest) can be obtained for the conditions investigated for Cases 1 and 2 as well. For comparison [30], measured an average indoor particle concentration in Finnish office environments (N = 528; ≥0.5 μm: 1.9E+06 p/m³; ≥5.0 μm: 2.5E+04 p/m³). With the exception of Case 1 Class A and B, these outside conditions would be sufficient to achieve the highest Class levels for the investigated cases.

The presented results were obtained for a cleanroom with L1 air leakage class. As the case study cleanroom has its own specifics, it would be advisable to perform additional measurements in other cleanrooms of similar and better leakage classes, to confirm the outcomes. For lower air leakage class cleanrooms, more research is needed to assess the ingress of airborne contamination into them.

All three cases had a recovery time (100:1) within 15–20 min after changing the system back to the original ACR and pressure hierarchy (stage 3). This matches the requirements in GMP annex 1 [4]. The solution proposed in Ref. [16] would guarantee a further safety procedure to assure a clean restart of the cleanroom. Though the GMP annex 1 [4], and its currently available draft version [17], highly recommend to maintain a pressure hierarchy under all operational conditions, the overall outcome of the cases supports the ISO 14644-16 [14] standard which recommends to reduce the flow, or even turn it off, in the non-operational periods (at rest). The guide recommends taking the following three risks into account for airborne particle control by DCF to 0 h⁻¹:

1. ‘Ingress of airborne contamination due to loss of pressurization in the classified space.’
2. ‘The ability to restore the required cleanliness conditions upon restarting the system within a determined recovery time related to the emission risk and period of turn off.’
3. ‘Deposition of contamination shaken from the clean side of the terminal high-efficiency filters.’

In this research, Risk 1 and 2 have been investigated. Risk 1 is mitigated if particle concentration conditions are limited to the concentrations as presented in Table 7. Recovery time, Risk 2, was confirmed to be in line with the requirements set [4]. Risk 3, deposition of contamination, was not measured in these experiments. The available setup was not able to measure particle deposition in the cleanroom during the non-operational hours or the behavior of the deposited particles after changing the flow back to its original settings. The sample time of the particle counters was too long to determine if deposited particles affect the cleanroom in the first few moments after the restart. Resuspended particles, however, may be treated as a temporary particle source in that case. In combination with the standard cleanroom ventilation conditions (high ACR and pressure differential), one may expect that they will be removed from the cleanroom quickly after restart of the system. Results from Ref. [7] indicate that current cleanroom HVAC systems are generally oversized and both during rest and in operation achieve a higher cleanliness class than required. This assumes some resilience with respect to handling resuspension. Oversizing results from conservative assumptions with respect to the particle sources present in the cleanroom when in operation. It is however advised to investigate the effects of particle deposition in the context of applying

![Fig. 5. Boxplots of the relative contamination (see Equation (1)) for Case 1, for the different particle sizes investigated, as function of the averaged samples (data points). The boxplots contain data points for all the measurements performed for Case 1 (three measurement series). The sample number refers to the group of samples as described in Section 2.4.](image-url)
The temperature conditions in the investigated cleanroom, as represented in Table 5, show that temperature differences between the air and cleanroom construction exist. For the walls, the difference however is in the order of 1 K or smaller and nearly within measurement accuracy. These small differences are expected as the cleanroom itself is not conditioned and has no additional insulation. As the cleanroom is positioned directly at the floor, here temperature differences are larger due to the thermal mass of the floor. The cleanroom floor therefore remains cooler. Due to this, mixing of air in the cleanroom will be reduced in the case of no ACR. At 4 h⁻¹ ACR, one may expect that the effect of the lower floor temperature will not affect the mixing of air in the cleanroom. For a heated floor, buoyant driven air velocities at these temperature differences would still remain in the order of 0.1 m/s and lower [31]. For a cold floor, these values are even lower.

### Table 5

Maximum temperature gradient in [K] between air and surface for the different measurement series. The air temperature was averaged from the supply and exhaust temperature, together with the air temperature measured at PC2. The maximum temperature difference between the air temperature at PC2 and the supply is also presented.

| Case 1 | Case 2 | Case 3 |
|--------|--------|--------|
| Air-floor [K] | Air-wall [K] | PC2-supply [K] | Air-floor [K] | Air-wall [K] | PC2-supply [K] | Air-floor [K] | Air-wall [K] | PC2-supply [K] |
| series 1 | 0.32 | 0.36 | 0.77 | 2.33 | 0.82 | 0.25 | 2.49 | 0.98 | −0.09 |
| series 2 | 0.82 | 0.34 | 0.82 | 2.82 | 0.68 | 0.45 | 2.67 | 0.91 | −0.02 |
| series 3 | 1.21 | 0.27 | 0.81 | 0.94 | 0.29 | 2.23 | 3.62 | 0.88 | 0.55 |

### 4.2. Energy savings

The measured energy savings potential for the cases investigated indicate a more than 70% reduction in fan energy demand when applying the Case 1 operating conditions (see Table 6). It does assume a situation where contaminant build-up in the weekend may take place for the Case 1 conditions. Such a long build-up was not investigated, though it can be expected that the outside load on the cleanroom will reduce in due course, assuming that during this period, no sources would be present outside the cleanroom as well. With that, the outcomes are expected to remain close to the results obtained for Case 1. Applying a 7-day operation week would however still result in energy savings in the order of 60%. Savings of similar order of magnitude were reported by Ref. [19]. Also, operating conditions with a reduced flow and pressure hierarchy are able to result in significant savings. As the air quality conditions, assuming the restrictions described, are not compromised, these savings may be easily obtained. These results thus advocate the use...
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of DCF in cleanroom applications.

4.3. Study limitations

Deposition and resuspension of particles were not measured in this research. The cleanroom was cleaned at the start of every experiment. The results of restarting the cleanroom after flow reduction (stage 3) assumes that resuspended particles are dealt with by the ventilation. It, however, remains unclear what fraction of deposited particles get resuspended.

The study only examined non-viable, airborne particles. GMP classified rooms also require control of CFUs (Colony Forming Units). Therefore, further research may focus on the relationship between flow reduction and CFUs. This would refer to CFU concentration build-up due to outside sources and to development (growth) of CFUs inside the reduction and CFUs. This would refer to CFU concentration build-up due to development (growth) of CFUs inside the reduction and CFUs. Therefore, further research may focus on the relationship between flow reduction and CFUs. This would refer to CFU concentration build-up due to development (growth) of CFUs inside the reduction and CFUs.

For the case study and DCF-conditions investigated, turning off the fan in the non-operational hours of a cleanroom (ACR = 0 h⁻¹; pressure difference = 0 Pa) in case of DCF does not jeopardize the quality of the cleanroom when particle concentration conditions outside the cleanroom are in line with normal conditions. A small air change rate (4 h⁻¹) or overpressure (7.5 Pa) already suffice to secure the quality further and guarantee air quality conditions at the highest GMP/ISO cleanroom contamination class. The application of the approach can result in fan energy savings in the order of 30%–70%. These outcomes would be supported by similar type of measurements in other cleanrooms.

5. Conclusion

For the case study and DCF-conditions investigated, turning off the fan in the non-operational hours of a cleanroom (ACR = 0 h⁻¹; pressure difference = 0 Pa) in case of DCF does not jeopardize the quality of the cleanroom when particle concentration conditions outside the cleanroom are in line with normal conditions. A small air change rate (4 h⁻¹) or overpressure (7.5 Pa) already suffice to secure the quality further and guarantee air quality conditions at the highest GMP/ISO cleanroom contamination class. The application of the approach can result in fan energy savings in the order of 30%–70%. These outcomes would be supported by similar type of measurements in other cleanrooms.

Declarations of competing interest

At the time the research was performed, co-authors van den Oever, Molenaar and Joosten were employed by Kuijpers PHF Services B.V., which is a company designing cleanrooms. Co-author Ludlage was employed by Kuijpers PHF Services B.V. after the research was finalized.

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Annex

Figure A.1. Boxplots of the relative contamination for Case 2 (left) and 3 (right) for the different particle sizes investigated as function of the averaged samples (data points). The boxplots contain data points for all the measurements performed for Case 2 and 3 respectively.

Table A.1
Summary of the relative contamination for the cases investigated. The results shown provide the numerical outcomes for the boxplots presented in Fig. 6 for the 2.5%, 25%, 50%, 75% and 97.5% quantiles.

| Case 1 Relative Contamination | 0.025 | 0.25 | 0.5 | 0.75 | 0.975 |
|------------------------------|-------|------|-----|------|-------|
| Quantile                    |       |      |     |      |       |
| ≥0.3 μm                     | 1.9E-02 | 2.1E-02 | 2.5E-02 | 2.6E-02 | 2.9E-02 |
| ≥0.5 μm                     | 2.0E-02 | 2.9E-02 | 3.3E-02 | 3.9E-02 | 4.3E-02 |
| ≥1 μm                       | 2.0E-02 | 3.0E-02 | 3.5E-02 | 4.1E-02 | 5.6E-02 |
| ≥3 μm                       | 1.3E-02 | 2.1E-02 | 2.1E-02 | 2.9E-02 | 2.1E-02 |
| ≥5 μm                       | 7.5E-03 | 1.2E-02 | 1.2E-02 | 2.1E-02 | 4.7E-02 |

| Case 2 Relative Contamination | 0.025 | 0.25 | 0.5 | 0.75 | 0.975 |
|------------------------------|-------|------|-----|------|-------|
| Quantile                    |       |      |     |      |       |
| ≥0.3 μm                     | 0.0E+00 | 0.0E+00 | 0.0E+00 | 0.0E+00 | 0.0E+00 |
| ≥0.5 μm                     | 2.5E-07 | 3.2E-07 | 3.6E-05 | 4.1E-07 | 4.1E-04 |
| ≥1 μm                       | 0.0E+00 | 0.0E+00 | 0.0E+00 | 0.0E+00 | 0.0E+00 |
| ≥3 μm                       | 3.5E-05 | 2.4E-04 | 1.9E-04 | 2.9E-04 | 2.4E-05 |
| ≥5 μm                       | 0.0E+00 | 0.0E+00 | 0.0E+00 | 0.0E+00 | 0.0E+00 |

| Case 3 Relative Contamination | 0.025 | 0.25 | 0.5 | 0.75 | 0.975 |
|------------------------------|-------|------|-----|------|-------|
| Quantile                    |       |      |     |      |       |
| ≥0.3 μm                     | 0.0E+00 | 0.0E+00 | 0.0E+00 | 0.0E+00 | 0.0E+00 |
| ≥0.5 μm                     | 0.0E+00 | 0.0E+00 | 0.0E+00 | 0.0E+00 | 0.0E+00 |
| ≥1 μm                       | 0.0E+00 | 0.0E+00 | 0.0E+00 | 0.0E+00 | 0.0E+00 |
| ≥3 μm                       | 0.0E+00 | 0.0E+00 | 0.0E+00 | 0.0E+00 | 5.8E-06 |

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