The application of the ventilation equations to cleanrooms – Part 2: Decay of contamination

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Abstract

This article is the second of a three-part series that investigates the application of the ventilation equations to designing and testing cleanrooms. This part is concerned with the decay equation. The recovery test, described in ISO 14644-3 (2005) is discussed, and improvements recommended. The application of the decay equation to the 'clean up' requirement given in the EU GGMP (2008) is also discussed. Finally, a method is considered that calculates the time needed for airborne contamination in cleanroom areas to decay to acceptable concentrations.

Introduction

In the first of a three-part series of articles, the ventilation equations used to calculate the build-up, steady-state and decay of undesirable gases in ordinary ventilated rooms, such as offices, were modified for cleanrooms (Whyte et al, 2012). The ventilation equations assume good air mixing, and should only be used with non-unidirectional airflow cleanrooms. This article considers the role of the decay equation in the cleanliness recovery test given in ISO 14644-3: 2005, the 'clean up' requirement in EU GGMP (2008), and the time required in a cleanroom areas for airborne contamination to decay to a required concentration.

The decay equation can be used to investigate the decay of airborne contamination when personnel leave a cleanroom, or machinery is switched off, and the concentration of contamination decreases in an exponential manner to a new steady state concentration, or zero. The following equation calculates the concentrations during decay.

Equation 1

$$C = C_I . e^{-N_V}$$

Where:
C = airborne concentration of particle contamination after a given decay time,
C_I = initial concentration of particles,
N_V = air change rate, t = elapsed time.

The air change rate (N_V) can be calculated by the commonly used equation:

Equation 2

$$N_V = \frac{air\ volume\ supply\ rate\ to\ cleanroom}{volume\ of\ cleanroom}$$

Figure 1 shows the exponential decay of airborne particles in three cleanrooms, as calculated by Equation 1, when the air change rates per hour are 20, 40 and 80, and good air mixing assumed. It should be noted that the rate of decay is dependent on air change rate. Therefore, in any cleanroom with the same air change rates and good air mixing, airborne contamination will decay at an identical rate.

Equation 1 can be solved for N_V, which is the air change rate at the measuring location.

Equation 3

$$N_V = -\frac{1}{t} ln \frac{C}{C_I}$$

or, when logarithms to the base 10 are used,

Equation 4

$$N_V = -2.3 \times \frac{1}{t} log_{10} (\frac{C}{C_I})$$

Equations 3 and 4 are based on the assumption that all the particles in the supply air are removed by the cleanroom's high efficiency filters, and that a pressurised cleanroom prevents infiltration of contamination from adjacent areas.

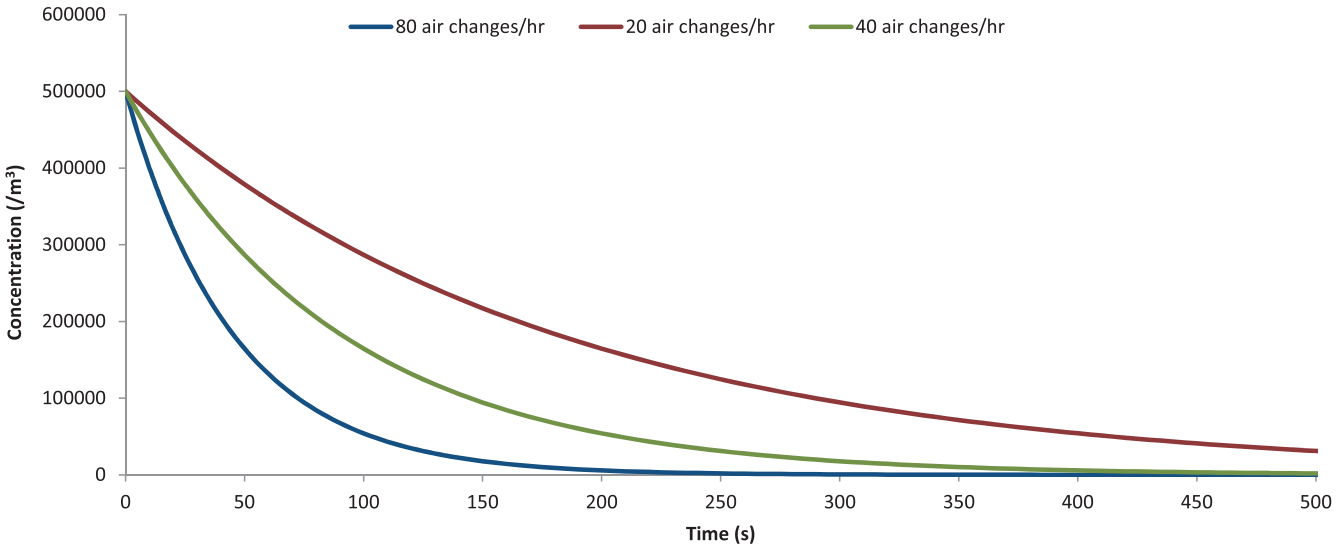

Figure 1: Decay of airborne particles with respect to air changes per hour

The above equations assume that particles remain suspended in the air and will therefore give good results when applied to particles ≥0.5µm. However, microbe-carrying particles (MCPs), which are normally dispersed by personnel on skin cells, have an average aerodynamic particle diameter of about 12µm (Whyte and Hejab, 2007) and settle under the influence of gravity at a deposition velocity of about 4.6 x 10^{-3}m/s (Whyte, 1986). The MCPs in cleanroom air are therefore deposited onto surfaces such as machinery and the floor, and this increases the apparent air change rate for MCPs by between 5 and 7 air changes per hour (Whyte et al, 2012).

Colebrook et al, (1948) has shown that decay mechanisms that cause a die-away or removal of contamination in an exponential way, such as by irradiation, airborne chemical disinfection, and surface deposition of particles, can be individually represented by a decay rate that has an exact equivalence to the removal rate obtained by a given air change rate. These different decay rates can be added together and Equation 1 can be modified to take account of the equivalent air change rate caused by losses in microbial concentration by surface deposition,

Equation 5

$$C = C_I \,.\, e^{-(N_V + N_D)t}$$

Where, N_V is the air change rate owing to ventilation, and N_D is the equivalent air change rate owing to surface deposition.

The equivalent air change rate owing to surface deposition (N_D) is exactly the same as the decay rate caused by surface deposition, and calculated as follows:

Equation 6

$$N_D = \frac{V_D . A}{V}$$

Where, V_D is the average deposition velocity of airborne particles onto surfaces (m/s), A is the horizontal deposition area (m^2), and V is the volume of the room (m^3).

The floor can normally be assumed to be the area of deposition, and therefore,

Equation 7

$$N_D = \frac{V_D}{H}$$

Where, H is the height of the room.

The above equations are used in the next few sections of this article to investigate the following cleanroom situations:

1. The cleanliness recovery test given in ISO 14644-3: 2005,
2. The method given in the EU GGMP (2008) for the 'clean up' of airborne contamination,
3. Calculation of the time required in cleanroom areas for airborne contamination to decay to required concentrations.

ISO 14644-3 cleanliness recovery test

Calculating the cleanroom recovery rate, air change rate, and ventilation effectiveness

ISO 14644-3: 2005 suggests two cleanliness recovery performance tests for ascertaining the ability of a non-unidirectional airflow cleanroom to eliminate airborne particles. The first test measures the recovery time for test particles to decay to 1/100 of their initial concentration. The second test evaluates the 'cleanliness recovery rate', which is the decay rate (N) of the test particles calculated by the following equation given in ISO 14644-3, where it is referred to as Equation B12.

$$N = -2.3 \times \frac{1}{t} log_{10}\left(\frac{C}{C_I}\right)$$

It can be seen that Equation B12 is identical to Equation 4, which is used to calculate the air change rate at a location in a cleanroom. The 'cleanliness recovery rate' obtained from Equation B12 is therefore identical to the 'air change rate' at the location where decay measurements are made.

The usefulness of the ISO 14644-3 cleanliness recovery tests is limited, as no method is given to decide whether the result obtained is satisfactory, or not. However, if the cleanliness recovery rate i.e. the air change rate at the measuring location, is compared with the cleanroom's average air change rate, an Air Change Effectiveness (ACE) Index of the type described by ASHRAE Standard 129 (2002) can be obtained by the following Equation 8. This method is discussed in detail by Whyte et al (2014), and the application of the method to diffuser performance in cleanrooms is reported by Lenegan (2014).

Equation 8

$$\text{ACE} = \frac{\text{air change rate at a test location}}{\text{average air change rate in the cleanroom}}$$

If the cleanroom air is perfectly mixed, the ACE will have a value of 1 at all locations, and an even concentration of airborne contamination throughout the cleanroom. If the ACE is greater than 1, more clean air supply will have reached the test location than average, and the recovery rate will be greater and the particle concentration lower. If the ACE is lower than 1, the opposite is true.

Measurement of decay rate, air change rate, and ACE index

The cleanliness recovery rate test given in ISO 14644-3:2005 is carried out by measuring the decay in concentration of test particles introduced into a cleanroom. These particles should be well mixed with cleanroom air, and the airflow pattern re-established before measurements are made. This can be achieved by switching

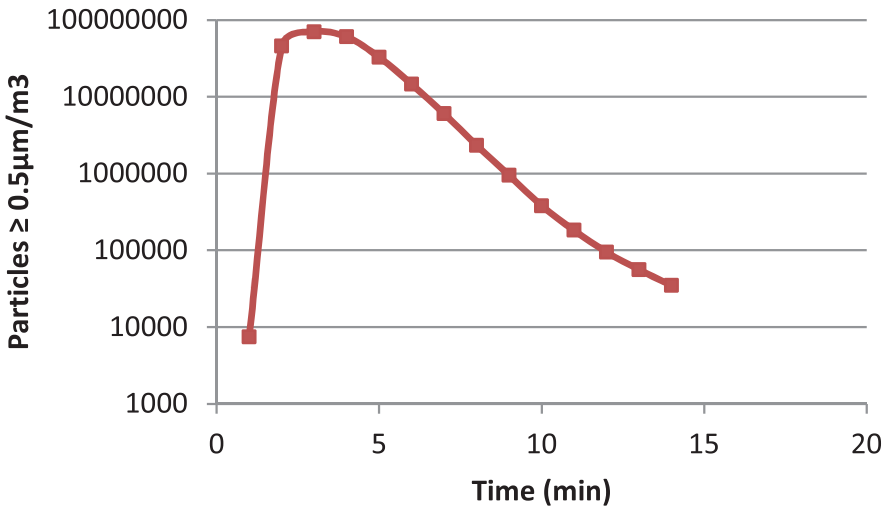

Figure 2: Decay of test particles ≥0.5µm in a cleanroom

off the air supply, thoroughly mixing the introduced particles with a fan, switching the ventilation back on, and allowing the air flow pattern to re-establish itself. However, it is very common to find that the air supply cannot be shut off, and particles are introduced when the air supply is running; these circumstances are discussed below.

ISO 14644-3 requires the size of particles to be <1 µm, and particles ≥0.5µm are normally measured, as this is the size also used in the EU GGMP 'clean up' test.

Shown in Figure 2 is a typical plot of the rise and fall of the concentration of particles introduced into a non-unidirectional airflow cleanroom when the air supply is running. The Y axis has a logarithmic scale. A few seconds burst from a single Laskin nozzle aerosol generator fed with Shell Ondina EL oil was used to introduce the test particles, and the generator then turned off. The airborne concentration, at the introduction of particles, is normally greater than zero because of the background concentration of particles in the cleanroom. There is then a rise in concentration caused by the introduction of test particles and a settling-down period when they mix with cleanroom air.

The highest particle concentration shown in Figure 2 is around the 'settling down' period, and almost $10^8/m^3$. This high concentration can be useful, as the delay needed for the test particles to drop to the concentration that can be accurately measured by a particle counter also gives the particles time to mix into the air and achieve a more even concentration.

Care must be taken to avoid optical coincidence losses in the particle counter. When the particle concentration is high, two or more particles in the sensor's light beam may cause the scattered light to be interpreted as a single larger particle, and this will result in a lower count. ISO 21501-4 (2007) requires the particle counter's concentration limit to be ascertained. This limit occurs when the coincidence loss becomes greater than 10% of the total count. Test readings should not be taken above the 10% coincidence loss concentration, or alternatively, a diluter used to reduce the concentration of particles in the air sample.

After mixing and settling-down, the particle concentration decays in an exponential manner, as confirmed by a straight line when the particle concentration is plotted logarithmically. Finally, at lower particle concentrations, the decay rate slows down, owing to background particle contamination caused by, for example, test personnel; these results should not be included in the calculation.

The decay rate, which is equal to the air change rate at the test location, should be calculated from only the results on the straight line portion of the graph in Figure 2, and can be obtained from the initial concentration (C_i), the concentration (C) after an elapsed time interval (t), and use of Equation 3 or 4. Alternatively, it can be obtained from the slope of the plot of the logarithm of the particle concentration over time. The ACE index is then calculated by Equation 8, where the average air change rate per hour over the whole cleanroom can be obtained by dividing the air supply to the room (m^3/h) by the volume of the room (m^3). Alternatively, the average air change rate of the cleanroom can be obtained by measuring the decay rate at each cleanroom air exhaust and obtaining a weighted average based on individual extract volumes.

Cleanroom ACE indexes

ACE indexes have been measured in a variety of cleanrooms and reported by Whyte et al (2014). The effect of an air diffuser on the airflow in one cleanroom was shown by measuring the ACE indexes at three locations in the cleanroom. These were one metre from the floor and a) below the air inlet, b) above the table and c) between the table and the extract air grille. The locations are shown in Figure 3, along with the airflow directions and velocities in the cleanroom when no diffuser was fitted to the air inlet.

The results are given in Table 1, where it may be seen that under the air supply inlet, when no diffuser is fitted, 1.8 times more clean air reaches the test location than the room average, but there is less clean air in the other locations. When a 4-way-throw diffuser is fitted, good air mixing was obtained in the room, as evidenced by the similarity of the ACE indexes measured at the three locations.

Twenty-three non-unidirectional airflow cleanrooms were also studied. Eleven were of the positive-pressure type and supplied with HEPA filtered air from 4-way-diffusers in the ceiling, and air extracted at low level. The mean value of the ACE indexes was 0.93, with a range of values between 0.67 and 1.28. Two cleanrooms were found to have an ACE index below 0.75. One of these was considered to be caused by obstructions

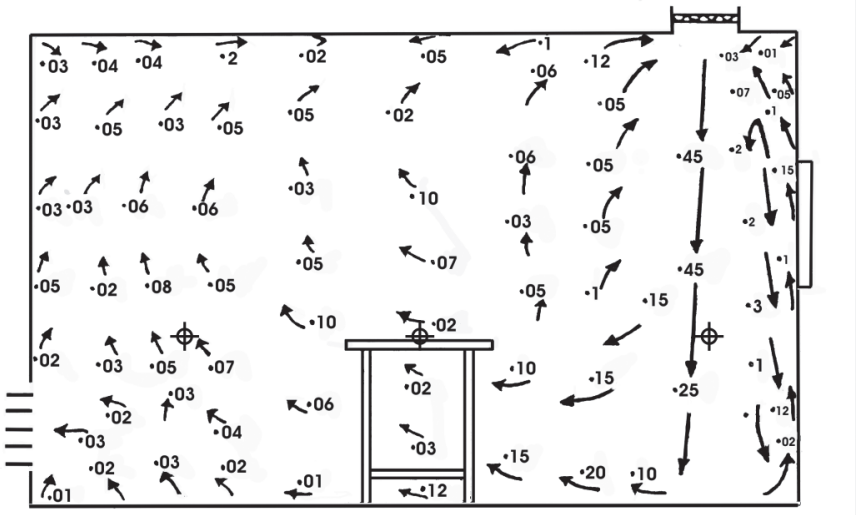

Figure 3: Sampling locations and airflow from air inlet without diffuser. Sampling position = ⊕

Table 1: The effect of air inlet diffusers on ACE indexes

Use of air inlet diffuser	Measuring location of ACE index		
	Below air inlet	Above table	Between table and air extract grille
No diffuser	1.8	0.87	0.68
Diffuser fitted	1.09	1.04	1.02

from large items of equipment but it was not possible to reinvestigate the other cleanroom.

A further 12 cleanrooms were investigated that were either cascade-type, or negatively-pressurised cleanrooms. These gave an ACE index above 1, owing to additional clean air being either drawn into the room in the case of negatively-pressurised cleanrooms, or passing through the room in the case of 'cascade' type cleanrooms. The reasons for the deviations of the ACE index from 1, in this and other situations, is discussed by Whyte et al (2014).

EU GGMP 'clean-up' method

The EU GGMP (2008) suggests that pharmaceutical cleanrooms used in aseptic production should recover quickly from high concentrations of airborne contamination. It suggests that for the grade of cleanroom being considered that 'the particle limits given in the table for the 'at rest' state should be achieved after a short 'clean up' period of 15-20 minutes (guidance value) after completion of operations. Testing cannot be carried out in Grade A areas as these usually have unidirectional airflow, but can be in Grade B and C areas, which normally have non-unidirectional airflow. Grade D areas cannot be tested, as the 'in operation' state is not defined.

There is no method given in the EU GGMP to ascertain the 'clean up' time but the common approach, which best fits the stated requirements, is to measure the concentration of naturally occurring particles ≥0.5µm immediately after production has stopped and personnel have departed. The particle concentration is then measured until the specified concentration of the 'at rest' state is reached, and the time noted.

The decay equation can be used to determine the excepted air change rate or 'clean up' time when the other variables are known. An example of the calculation of the air change rate is now given. In EU GGMP Grade B and Grade C areas, the maximum concentration of particles ≥0.5µm allowed during operation is 352,000/m^3 and 3,520,000m^3, respectively, and these concentrations can be considered to be the worst condition immediately after operations have ceased. The 'at rest' concentrations that should be achieved at the end of the 'clean-up' test in a Grade B area is 3520/m^3, and in a Grade C it is 352,000/m^3. The shortest suggested decay time of 15 minutes is the most challenging, and this time is used here.

Using Equation 4, the air change rate (N) required to produce the required particle decay in 15 minutes in a Grade B cleanroom, when there is good air mixing, i.e. the ACE is close to 1, can be calculated as follows:

$$N = -2.3\times\frac{1}{t}\log_{10}\left(\frac{C}{C_I}\right)$$
$$= -2.3\,\frac{1}{15}.\log_{10}.\frac{3520}{352000}$$
$$= 0.31/\text{min} = 18.4/\text{hour}$$

Similarly, for a Grade C area:

$$N = -2.3\times\frac{1}{t}\log_{10}\left(\frac{C}{C_I}\right)$$
$$= -2.3.\frac{1}{15}.\log_{10}.\frac{352000}{3520000}$$
$$= 0.15/\text{min} = 9.2/\text{hour}.$$

Decay of airborne contamination to a required concentration in cleanroom areas

In addition to the EU GGMP 'clean-up' test explained in the previous section, there are other situations in cleanroom areas where a decay of airborne contamination to an acceptable condition is required. For example, the airborne contamination in an airlock may need to be quickly reduced before a single or double door is opened into an adjoining higher-quality cleanroom. Another application is in cleanrooms where energy is saved by reducing the air supply rate when the cleanroom is not being used e.g. overnight or the weekend, and appropriate recovery times for returning to normal operational conditions need to be determined. The requirements for both these applications, and other similar situations, can be calculated by the decay equation.

Airlocks act as a buffer to prevent airborne contamination entering cleanrooms, such as production cleanrooms, which require low levels of airborne contamination. Airlocks are ventilated with HEPA-filtered air to control their airborne contamination, but they may have high concentrations of contamination coming from less-clean zones when the adjoining door is opened, or from the unwrapping and decontamination of materials during activities in the airlock. The opening of the door into the higher quality cleanroom should therefore be delayed until contamination is reduced to an acceptable level. The following example shows how the time may be calculated.

An airlock is being designed to transfer items into a cleanroom. It is thought that the floor area should be about 20m^2 with a ceiling height of 3.2m i.e. a volume of 64m^2. The airborne concentration of particles ≥0.5µm in the airlock when personnel leave and the materials are ready for transfer, is assumed to be 500,000/m^3.

Figure 1 shows the decay of particles in the air lock as calculated by Equation 1, when air change rates per hour are 20, 40 and 80, and good air mixing assumed i.e. an ACE index of about 1. Towards the end of the decay, the concentration becomes asymptotic to the axis and will theoretically never reach zero. A practical solution to this is to accept a concentration of 5% of the original concentration as the end point. The time for particles to decay to 95% of the original concentration i.e. to 25,000/m^3 is calculated by the following rearranged Equation 3.

Equation 9

$$t = \frac{1}{N_V} ln \frac{C}{C_I}$$

Using Equation 9, the time required to achieve a 95% decay of particles ≥0.5µm for 20, 40 and 80 air changes per hour is calculated and given in the second column of Table 2.

The decay of MCPs in an airlock will be faster than for particles ≥0.5µm, because of losses caused by gravitational deposition onto surfaces. If an airlock is installed in a pharmaceutical or medical devices cleanroom where MCPs are the most important contaminant, this can be

Table 2: Times required to achieve a 95% reduction in particles ≥0.5µm and MCPs

Number of air changes (N_V)	Time for airlock to reach a 95% reduction in particles ≥0.5µm (s)	Time for airlock to reach a 95% reduction in MCPs (s)
20	540	429
40	270	239
80	135	127

taken into consideration. In our example, the height of the cleanroom is 3.2 m, and the deposition velocity of MCPs is assumed to be 0.0046m/s. Therefore, the equivalent air change rate caused by surface deposition can be calculated to be 5.2/h by using Equation 7 as follows:

$$N_D = V_D/H = 0.0046/3.2 * 3600 = 5.2/h$$

To obtain the new shorter recovery time for MCPs, the equivalent air change of 5.2/h should be added to the air change rate arising from the air supply, and the calculation using Equation 9 repeated. These results are given in the third column of Table 2.

An alternative approach to calculating the air supply rate of an airlock is to decide what concentration is required in the airlock before the door to the higher-quality cleanroom is opened. If, for example, the adjacent higher-quality cleanroom is EU GGMP Grade B with a maximum particle contamination of 352,000/m^3, the airlock can be designed to achieve this concentration before the door is opened. If the initial particle concentration of particles ≥0.5µm is again assumed to be 500,000/m^3, it can be calculated by Equation 9 that the airlock should be ventilated for 64s, 32s and 16s when 20, 40 and 80 air change per hour, respectively, are utilised.

It is also possible to set a recovery time and calculate the required air change rate. If, for example, the recovery time is set at 180s to achieve a 95% decay of the initial concentration, the air change rate can be calculated to be 60/h using Equation 3 as follows:

$$N = -\frac{1}{180}.\ln\frac{25000}{500000}. = 0.017/s = 60/h$$

Equation 2 shows that reducing the volume of the airlock, when the air supply rate remains constant, increases the air change rate in direct proportion. Therefore, if the volume of the airlock was reduced from 64m^3 to 50m^3, the 22% reduction in volume will give a 22% increase in the air change rate, and shorten the decay time by the same percentage.

If the best design for the required air lock is now considered with respect to optimising the time to transfer items into the cleanroom, the first choice might be an airlock where the particle concentration is reduced by 95% in 270s by using an air change rate of 40/h. However, if a reduction of the airlock volume by 22% is considered acceptable, the increased air change rate of 48.8/h gives a useful time reduction to 221s. If MCPs are considered to be the relevant contaminant, and the equivalent air change rate of 5.2/h added to give an air change rate of 54/h, the recovery time becomes 200s. A traffic light indication-system can be installed to show when the 200s is reached and the interconnecting door may be opened for items to be transferred into the production room.

Discussion and Conclusions

This article considers the application of the ventilation decay equation to cleanrooms and, in particular, to the recovery methods given in ISO 14644-3, the 'clean-up' requirement in the EU GGMP, and the time required to achieve a required reduction of airborne contamination in cleanroom areas.

Cleanliness recovery methods to determine the ability of a cleanroom to eliminate airborne particles are given in ISO 14644-3: 2005. Two methods are suggested: one method measures the time for test particles to drop to 1% of the initial concentration, and the other measures the rate of decay. Information given in this article, and as well as the investigations reported by Whyte et al (2014), allows the following conclusions to be drawn.

The '100:1 recovery time' and the 'recovery rate' tests measure the same fundamental property i.e. rate of decay of airborne contamination. However, measuring the time to achieve 1% of the concentration is often carried out without plotting the results, and may therefore include results at the beginning and end of the collection period,. These results do not decay in an exponential manner and hence the recovery time will be inaccurate. However, measuring and plotting the 'recovery rate' allows results to be taken from the exponential part of the decay plot and, consequently, more accurate results to be obtained. Also, importantly, using the recovery rate method allows an ACE index to be calculated. It is therefore recommended that the recovery rate method should be the preferred method in ISO 14644-3: 2005.

A common method used to measure the ISO 14644-3: 2005 recovery rate is to take decay measurements in the middle of the room and assume that the result is applicable to the whole room. It is clear from the experiments reported in this paper that this cannot be assumed. If, for example, measurements are taken under an air terminal not fitted with a diffuser, the downward flow of clean air would give a recovery rate much greater than the average in the room. The results obtained by the recovery methods must therefore be considered to apply only to the test location.

The ISO 14644-3: 2005 recovery rate test does not give a method to assess whether the result obtained from the test is satisfactory, or not. However, it has been shown that the 'recovery rate' is identical to the 'air change rate' at the test location. Understanding this fact and that the units of measurement of the recovery rate are 'air changes per unit of time', allows an assessment of cleanroom performance at important locations in the cleanroom. This is done by comparing the measured local air change rate with the overall air change rate in the cleanroom, and calculation of an ACE index. Calculation of the ACE index gives additional insight into room performance, and shows whether the recovery rate at a particular location is higher or lower than average, and whether the concentration of airborne contamination is also likely to be higher or lower. It is therefore a key recommendation of this paper that calculation of the ACE should be included in the recovery rate method given in ISO 14644-3: 2005. This test would be particularly useful in testing cleanrooms when first built, or when major changes have occurred.

ACE indexes greater than 1 are acceptable in cleanrooms as they show that the airborne contamination will be lower than average. However, if the ACE index drops below 1, airborne concentrations may be higher than desired, and it is suggested that if the value of the ACE index drops below 0.7 the reason for low results should be determined. If a retest confirms the result, then the airflow pattern in the room should be investigated using the airflow visualisation tests suggested in ISO 14644-3 to ensure no adverse air movements could lead to potential product contamination. Although ACE indexes greater than 1 need not be investigated, it should be understood

that higher values are likely to be associated with low ACE indexes in other parts of the cleanroom. A list of the reasons for the deviations of the ACE index from 1, has been given by Whyte et al (2014).

The 'clean up' requirement given in the EU GGMP (2008) was also investigated. Use of the decay equations shows that if good air mixing can be assumed i.e. the ACE index is close to 1, the required decay of particles can be achieved in a Grade B non-unidirectional airflow cleanroom by an air change rate of about 18 /hour, and in a Grade C cleanroom by about 9 /hour. Obtaining an ACE index from the information generated during the EU GGMP 'clean up' test would require only a little additional effort, and it is recommended that this is added to the test method. Air change rates and ACE indexes in a number of different locations, including critical locations, can also be determined by using the techniques reported in this paper.

Decay equations can be used to design areas where a controlled reduction in the airborne contamination is required, such as in air locks, or in cleanrooms where the air supply is temporarily reduced as an energy-saving measure when the cleanroom is not in use. The method for calculating an appropriate recovery time for contamination to drop to an acceptable concentration when normal operational conditions are re-established is described in this article.

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