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# The application of the ventilation equations to cleanrooms

## Part 1: The equations

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### Abstract

This is the first article in a three-part series that considers the application of the 'ventilation equations' to the design and testing of the air supply systems of non-unidirectional airflow cleanrooms. By means of these equations, the 'build-up' and 'decay' of the concentration of airborne contamination in cleanroom areas can be established. The equations can also be used to determine the likely 'steady-state' airborne concentration of contaminants in the operational state, or the air volume supply rate required to ensure that the concentrations of airborne particles, or microbe-carrying particles, are not exceeded. The most suitable equations have been identified, and adapted for use with microbe-carrying particles, where surface deposition will affect the airborne concentration. These equations can also be used to recognise the key variables involved in establishing the airborne concentration of contamination in non-unidirectional airflow cleanrooms.

### 1 Introduction

The derivation and application of the 'ventilation equations' can be obtained in building services text books such as Jones (2002), and Eastop and Watson (1992). These equations are normally used to determine the concentration

of undesirable or toxic gases during the build-up, steady state, and decay, in ventilated rooms or buildings, in the manner shown in Figure 1.

The three stages of the concentration of airborne contamination i.e. 'build-up', 'steady state' and 'decay' are also found in non-unidirectional airflow cleanrooms. In an empty cleanroom, no airborne contamination is dispersed, and hence the airborne concentration of particles measured by conventional air samplers, and microbe-carrying particles (MCPs) will be close to zero. However, as personnel enter the cleanroom and move about, and machinery and equipment is switched on, the concentration of airborne contamination will 'build-up' until it reaches a 'steady-state' condition. The steady-state condition occurs when the rate of dispersion of contamination into the cleanroom air is balanced by its dilution and removal by the ventilation system. When machinery is switched off and personnel depart from the room, the airborne contamination will then 'decay' down to a new concentration which, in the case of an empty cleanroom, will be very close to zero.

The general ventilation equation that is used to calculate the airborne concentration of contaminants during any of the three stages of ventilation

is as follows:

#### Equation 1

$$C = (D/Q + C_B) \cdot (1 - e^{-(Q/V)t}) + C_i \cdot e^{-(Q/V)t}$$

Where,  $C$  = concentration of contaminants /m<sup>3</sup> in a room at a given time;  
 $D$  = release rate of airborne contaminant /s;  
 $Q$  = air volume supply rate (m<sup>3</sup>/s);  
 $C_B$  = background concentration of contamination /m<sup>3</sup> entering the room in the air supply;  
 $t$  = elapsed time (s);  
 $V$  = room volume (m<sup>3</sup>)  
 $C_i$  = initial concentration of contaminants /m<sup>3</sup> in a room.

Equations are available for calculating airborne concentrations during each of the individual stages, i.e. the build-up, steady-state and decay, and these are considered later in this article.

Good air mixing is assumed in the derivation of the ventilation equations, and hence they should not be used in unidirectional airflow cleanrooms. They can be used in non-unidirectional airflow cleanrooms of the type shown in Figure 2, where large quantities of supply air pass through high efficiency filters in the terminal position in the air supply ducts. The air then passes through ceiling diffusers, which ensure that the particle-free air is well mixed with contaminated air in the cleanroom (Whyte, et al 2011). Also shown in Figure 2 is the dispersion of airborne contamination from personnel and machines, and its dilution by the particle-free supply air and removal through low-level extracts. Some dispersion of contamination comes from the floor during walking, but a research article being prepared by the principal author of this paper will show that this is likely to be less than 1% of the airborne contamination found in a cleanroom. Taking into consideration the variability of the airborne concentrations in a room,

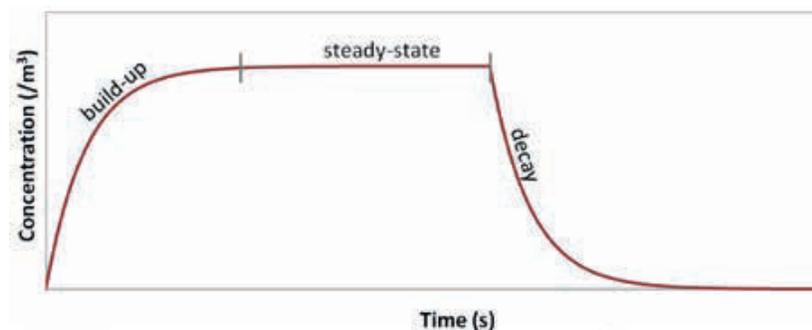


Figure 1: Build-up, steady state, and decay of airborne contamination in a ventilated room

it is reasonable to ignore this source of contamination. Also, the concentration of airborne contamination can be reduced through deposition of particles from the air onto surfaces, mainly the floor, but it is only the larger airborne particles, such as microbe-carrying particles (MCPs) that need to be considered.

## 2 Modification of the general ventilation equation for cleanroom use

### 2.1 Background contribution of contamination from air supply and room infiltration

The general Equation 1 has a background component 'C<sub>B</sub>' which is used when contaminants are additionally supplied to a room by means of the air supply. For example, carbon dioxide is dispersed in a room by people breathing, but additionally enters a room with the fresh air supply, and this additional carbon dioxide is considered 'background' contamination. However, in a cleanroom, air supply filters are used that have a very high particle-removal efficiency, and their integrity is routinely determined. This ensures that practically no particles, especially in the case of larger-diameter MCPs, pass into the cleanroom (Whyte et al, 2012). In addition, the air supply and extract volumes are slightly imbalanced, so that more air is supplied than is extracted, and the cleanroom is therefore positively-pressurised with respect to adjacent areas. The surplus air leaves through controlled gaps, such as

round the doors and through pressure relief flaps, or through uncontrolled gaps, such as those caused by poor construction or where services penetrate the room. This ensures that airborne contamination does not infiltrate through the cleanroom fabric from adjacent contaminated areas. Therefore, for all practical purposes, in a correctly commissioned and maintained cleanroom, the contribution of airborne particles from the supply air, or by infiltration from adjacent areas, can be assumed to be zero. As there is no other source of background contamination, the background concentration of contamination (C<sub>B</sub>) can be removed from the general ventilation Equation 1 to give the following Equation 2:

#### Equation 2

$$C = D/V(1 - e^{-Q.t/V}) + C_i.e^{-Q.t/V}$$

### 2.2 The use of air change rates

Air change rates, such as 20 room air changes per hour, are commonly used to describe the amount of air supplied to a cleanroom. The cleanroom's air change rate (N) is the number of room volumes of air supplied in a given time, and can be determined as follows:

#### Equation 3

$$N = Q/V$$

Therefore, in Equation 2, the cleanroom's air change rate 'N' can be substituted for 'Q/V', and the following general ventilation equation obtained,

#### Equation 4

$$C = (D/Q).(1 - e^{-Nt}) + C_i.e^{-Nt}$$

### 2.3 Adaption of the ventilation equations to include surface deposition

The ventilation equations discussed in text books are normally used in ordinary rooms and buildings to investigate the concentration of unwanted gaseous contamination. Although gaseous contamination can be a problem in cleanrooms, the main problem is with particles and, in the healthcare industries, MCPs. These contaminants may deposit from the air onto surfaces and therefore reduce the airborne concentration in the cleanroom. The significance of this effect requires investigation and, if shown to be important, an adaption of the ventilation equations is required.

As will be discussed later on in this article, the ventilation equations used in the individual stages of ventilation may include either the air change rate (N), or the air supply rate (Q), or both, and how the effect of surface deposition is incorporated into these two measurements of ventilation is now considered.

#### 2.3.1 Surface deposition using equivalent air change rate

When air change rates (N) are used in a ventilation equation, the equation can be modified to include the effect of other decay mechanisms using the approach discussed by Colebrook et al, (1948). 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. All these different decay rates can be added together to give a total equivalent air change rate. In our situation, the decay or removal of contamination may occur by two mechanisms, which are by ventilation and by surface deposition, and the air change rate (N) substituted as follows:

#### Equation 5

$$N = N_v + N_D$$

Where, N is the total equivalent air change rate

N<sub>v</sub> is the air change rate owing to ventilation,

N<sub>D</sub> is the equivalent air change rate owing to surface deposition

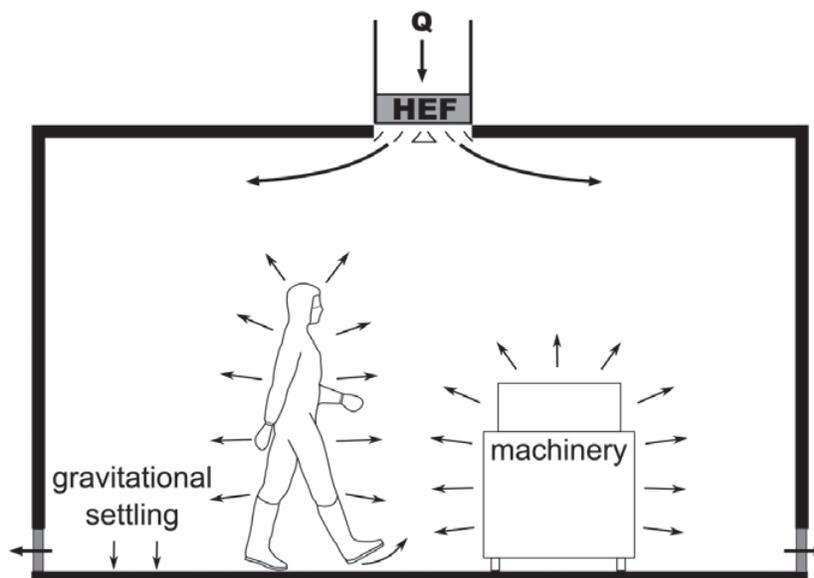


Figure 2 Airflow in a non-unidirectional airflow ventilated cleanroom. HEF = high efficiency filter

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

**Equation 6**

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

Where,  $N_D$  is the decay rate /s owing to surface deposition,  
 $V_D$  is the average deposition velocity of airborne particles onto surfaces (m/s),  
 $A$  is the horizontal deposition area (m<sup>2</sup>), and,  
 $V$  is the volume of the room (m<sup>3</sup>).

If the floor is the area of deposition surface, then,

**Equation 7**

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

Where,  $H$  is the height of the room.

### 2.2.2 Deposition using equivalent air supply rate

In the previous section, a modification was made to the air change rate to include the loss of particles owing to surface deposition. However, where a ventilation equation uses an air supply rate rather than an air change rate, it is convenient to include this additional deposition loss in terms of equivalent air supply rate ( $Q_D$ ).

The equivalent air change rate owing to surface deposition ( $N_D$ ) is shown in Equation 6 to be equal to  $V_D A/V$ . However, the equivalent air change rate ( $N_D$ ) is also shown in Equation 3 to be equal to  $Q_D/V$ , and hence,

$$\frac{Q_D}{V} = \frac{V_D A}{V}$$

By multiplying through by 'V'

**Equation 8**

$$Q_D = V_D A$$

As the term ' $V_D A$ ' is equal to  $Q_D$ , this term can be added to the ventilation air supply rate to obtain a total equivalent air supply rate that gives the same airborne reduction as obtained from both ventilation and surface deposition. This is discussed further in the Section 3 of this article.

### 2.2.3 Deposition velocity

There are a number of mechanisms that may cause particle deposition on surfaces, such as gravitational settling, Brownian diffusion, eddy diffusion, impaction and electrostatic effects; these

mechanisms are described by Hinds (1999). The importance of these deposition mechanisms has been extensively studied in cleanrooms e.g. Liu and Ahn, 1987; Wu et al, 1989; Pui et al, 1990, and Cooper et al, 1990. It has been shown that for particles greater than 1µm, gravitational settling accounts for most of the deposition in normal cleanroom conditions. For particles less than about 0.1µm, Brownian diffusion is the major deposition mechanism. In the intermediate size range both gravitational settling and Brownian diffusion act. Electrostatic attraction can also cause deposition in suitable circumstances, but the prediction of the amount of deposition can normally be calculated by consideration of only gravitational settling and diffusion. Actual deposition velocities in working cleanrooms have been determined by obtaining the surface deposition rate of particles onto test wafers at known concentrations of airborne contamination. Carr et al (1994) determined that for cumulative counts of airborne particles  $\geq 0.3\mu\text{m}$ , as measured by a conventional airborne particle counter, the average deposition velocity was  $3 \times 10^{-5}\text{m/s}$ . This velocity is in the range calculated theoretically, and measured experimentally by test particles (Liu and Ahn, 1987; Wu et al, 1989; Pui et al, 1990, and Cooper et al, 1990).

In pharmaceutical and healthcare cleanrooms, MCPs are the most important contaminant, and these have a much greater deposition velocity than particles  $\geq 0.3\mu\text{m}$ . The main, and normally only, source of MCPs in the cleanroom is people. Microbes grow on skin, and people shed about one layer of skin cells per day, which amounts to about  $10^9$  skin cells. Skin cells are about  $44\mu\text{m} \times 33\mu\text{m}$  in surface area, and about  $3\text{--}5\mu\text{m}$  thick, although they fragment when dispersed into the air (McIntosh et al, 1978). The dispersion of microbe-carrying skin cells has been shown to be the main source of microbes in the air of an occupied room (Davis and Noble, 1962). Experiments have shown that the main mechanism of deposition of MCPs is by gravitational settling (Whyte, 1981 and Whyte, 1986) and MCPs have an average deposition velocity of  $4.6 \times 10^{-3}\text{ m/s}$ , with an average equivalent particle diameter of about  $12\mu\text{m}$  (Noble et al, 1963; Whyte, 1986; Whyte and Hejab, 2007).

### 2.2.4 The effect of surface deposition on airborne concentration

The surface deposition of particles and MCPs will reduce the airborne concentration in non-unidirectional cleanroom, and this effect can be calculated in a practical situation to demonstrate its importance. Assuming a cleanroom's ceiling height is 3m, the decay rate per second owing to surface deposition can be calculated by means of Equation 5 or 6, and then converted to a decay rate/h. This result is exactly equal to the number of air changes per hour that would give the same reduction in airborne concentration. Particles  $\geq 0.3\mu\text{m}$ , with a deposition velocity of  $3 \times 10^{-5}\text{m/s}$ , can be calculated to give an equivalent air change rate of 0.036/hour. It is therefore reasonable to assume that the reduction in airborne contamination owing to the surface deposition of particles  $\geq 0.3\mu\text{m}$  (or  $\geq 0.5\mu\text{m}$ ), can be ignored in this situation. However, MCPs which will have an average deposition velocity of  $4.6 \times 10^{-3}\text{ m/s}$  will give an equivalent air change rate of 5.5/h and this is substantial enough to be included in the calculations.

## 3 Modification of the general ventilation equation for use in the three stages of ventilation in cleanrooms

### 3.1 Build-up

In an empty cleanroom, where there is no activity, the initial concentration of contamination ( $C_i$ ) can be assumed to be zero. The general Equation 1 can therefore be transformed to the following Equation 9 that can be used to calculate the build-up of particles in the air in the manner shown in Figure 1.

**Equation 9**

$$C = (D/Q)(1 - e^{-Nt})$$

Where there is significant deposition of particles onto surfaces, as in the case with MCPs, the methods described in section 2 can be used to adapt Equation 9 to give the following more accurate Equation 10:

**Equation 10**

$$C = (D/(Q + V_D A))(1 - e^{-(N_D + N_V)t})$$

It should be noted that the build-up of airborne contamination is determined by both the air supply rate and air change rates.

### 3.2 Steady State

When personnel enter an empty cleanroom and start work, the airborne concentration will build-up and then settle to a fairly constant 'steady-state' concentration, where the airborne dispersion of particles, or MCPs, is balanced by their dilution by the air supply and removal through the air extracts and, to a lesser extent, by deposition on surfaces. The airborne concentration may vary during the steady-state operational state, but an average concentration in the cleanroom can be calculated. This concentration is important, as it is the concentration to which product is exposed, and airborne concentrations that should not be exceeded are given in ISO 14644-1 (1999), EU GMP (2008) and the FDA Guidance (2004).

The steady-state equation is established by using the common mathematical approach of assuming that the time (t) in the general Equation 1 extends towards infinity, and hence,

#### Equation 11

$$C = D/Q$$

Equation 11 should be used when surface deposition is not important, such as when using a cumulative count of particles  $\geq 0.3$  (or  $\geq 0.5 \mu\text{m}$ ), as determined by a conventional particle counter. However, where surface deposition is important, as in the case of MCPs, an additional term should be added and the steady-state concentration calculated using the following equation:

#### Equation 12

$$C = D/(Q + V_D \cdot A)$$

Where,  $V_D$  is the deposition velocity, which in the case of MCPs is  $4.6 \times 10^{-3}$ , and,  $A$  is the horizontal deposition surface area ( $\text{m}^2$ ).

The horizontal deposition surface can be assumed to be equivalent to the area of the floor, unless there are sizable objects in the room that reach up to the ceiling.

It should be noted that both Equations 11 and 12 show that the steady-state concentration is determined by the room's air supply rate and not the air change rate. It is very common, when designing a ventilation system for cleanrooms, to specify air change rates and assume that these determine the operational concentration in cleanrooms. However,

this is not the case, as demonstrated by the following information.

The determination of the air change rate in a ventilated room is given in Equation 3 and, for an hourly rate, the following equation should be used:

#### Equation 13

$$N = \frac{Q}{V}$$

Where,  $N$  = air changes per hour,  $Q$  = air supply rate ( $\text{m}^3/\text{h}$ ), and,  $V$  = volume of room ( $\text{m}^3$ ),

Therefore,

#### Equation 14

$$Q = N \cdot V$$

Substituting the value of 'Q' from Equation 14 into Equation 11,

#### Equation 15

$$C = D/N \cdot V$$

Equation 15 shows that the steady-state airborne concentration in a cleanroom is dependent on both the air change rate and its volume, and therefore for two cleanrooms with the same air change rate but with different volumes, the airborne contamination will also be different. This may be illustrated further by a practical example.

Consider a small cleanroom with a floor area of  $6\text{m} \times 6\text{m}$  and a ceiling height of  $2.8\text{m}$  i.e. the room volume is  $100\text{m}^3$ . If the air changes are set at 20 per hour then, using Equation 13, it can be calculated that the air supply volume required to obtain 20 air changes per hour would be  $2016\text{m}^3/\text{h}$ . However, if the room was twice the original size i.e.  $200\text{m}^3$  then for the same air change rate of 20/h it would be necessary to supply twice the air volume i.e.  $4032\text{m}^3/\text{h}$ . There will, therefore, be twice the volume of air supply available to dilute and remove contamination, and hence the airborne concentration in the larger room will be half that of the smaller room for the same air change rate.

### 3.3 Decay

If all personnel leave the cleanroom and manufacturing ceases, there will be no contamination generated, and the airborne particle count will decay from the steady-state concentration in the exponential manner shown in Figure 1. The following decay Equation 16 will allow the decay concentration to be calculated and is derived from the general ventilation equation by assuming that the dispersion rate is zero.

#### Equation 16

$$C = C_i \cdot e^{-Nt}$$

Where,  $C_i$  = initial room concentration ( $\text{no./m}^3$ )

To take account of the additional decay of particles caused by surface deposition, the equivalent air change rate owing to surface deposition ( $N_D$ ) should be included in Equation 15 to give the following equation:

#### Equation 17

$$C = C_i \cdot e^{-(N_D + N)Vt}$$

It should be noted that the decay of contamination is determined by the air change rate, which is different from both the build-up and steady-state equations.

The decay of airborne contamination from a steady-state condition down to zero (or to a new steady-state condition) is asymptotic to the new condition. Because of the asymptotic decay, the concentration will, theoretically, take an infinite time to reach the new steady-state concentration. As will be shown in the third article of this three-part series, samples of the airborne concentration of particles and MCPs in cleanrooms are very variable, and it is therefore reasonable and practical to assume that when the decay of contamination has dropped to 95% of the original concentration, the steady-state has been reached.

## Discussion

This article discusses the application to non-unidirectional cleanrooms of the ventilation equations that are normally used in ordinary rooms and buildings to calculate the concentrations of undesirable or toxic gases. These ventilation equations are used to investigate the build-up, steady state, and decay of airborne contamination. With a little modification, and the inclusion of the effect of surface deposition, they can be used in non-unidirectional cleanrooms in the following situations:

1. Calculation of the rate of recovery of cleanrooms from airborne contamination;
2. Calculation of the rate of decay of airborne contamination in clean zones, such as an air lock;
3. Estimation of the expected concentration of airborne contamination in non-unidirectional cleanrooms;

4. Determination of the air supply volume required in non-unidirectional cleanrooms to obtain a required steady-state (operational) airborne concentration;

The methods given in ISO 14644-3 and EU GMP to measure the rate of decay, or recovery from airborne contamination in cleanrooms will be considered in the second companion article, along with the determination of the decay of contamination in clean areas, such as air locks. The calculation of the likely steady-state concentration, or the air supply volume required to achieve a required steady-state condition, will be discussed in the third article.

The ventilation equations show the key variables involved in the ventilation of cleanroom. For example, the build-up of contamination in a cleanroom depends on air supply rate, air change rate, and source strength of the emissions of airborne contamination. The steady-state concentration is dependent on only the air supply rate and the emission source strength, but not the air change rate. The decay of contamination is dependent only on the air change rate. Because of their comparatively large size, MCPs are deposited on surfaces by the action of gravity, and this surface deposition is equivalent to the dilution caused by a supply of particle-free air of about 5.5 air changes per hour. The effect of surface deposition of MCPs should therefore be incorporated in the ventilation equations to obtain a more accurate calculation. However, this is not considered necessary for cumulative counts of airborne particles  $\geq 0.3\mu\text{m}$  (or  $\geq 0.5\mu\text{m}$ ), as measured by a conventional airborne particle counter, as their size gives low rates of deposition.

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