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Clean Air and Containment Review is a quarterly journal aimed at users, specifiers, designers, manufacturers, installers and testers of clean air and containment equipment. It publishes articles of topical, technical and historical interest, updates on standards and regulations, news, views and information on relevant events, especially training.

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EUROMED communications
Passfield Business Centre, Passfield
Liphook Hampshire, GU30 7SB
T: +44 (0)1428 752222
F: +44 (0)1428 752223
e: publisher@euromedcommunications.com
www.euromedcommunications.com

Editorial

Welcome to CACR 35. This issue begins with a major article by Bill Whyte and Koos Agricola explaining the two mechanisms whereby various particles are removed from the air in cleanrooms, namely airflow and deposition. The article starts on page 4. Traditionally we have determined the cleanliness of a cleanroom by measuring the concentration of particles in the air. This can be done in real time near the product to be protected. But what really matters is how many of the particles actually deposit on the product and now there are instruments available that can measure particle deposition rates in real time near the product Not only that, but a standard for particle deposition rate is in the very early stages. Look out for ISO 14644-17!

In the next article, which starts on page 12, Alexander Fedotov challenges the statistical treatment for the classification of cleanrooms as set out in ISO 14644-1:2015 – Classification of air cleanliness by particle concentration. The disclaimer at the bottom right of this page applies to this article but the point is that CACR gives experts an opportunity to express their own views. As editor, I would be very happy to publish reasoned reactions to Alexander's article in future issues.

CACR 35 continues with a short paper on the removal of airborne contamination using hydrogen peroxide vapour – see page 16. Much has been published on surface decontamination as measured using biological indicators (BIs) and, more recently, enzyme indicators (EIs) as first described in CACR but here the work has been carried out with microbial air samplers. Still on the subject of hydrogen peroxide vapour, MHRA has very kindly allowed us to reproduce a blog written by Andrew Hopkins, Senior GMDP inspector at the MHRA. This blog (page 18) concerns the fragility of the hydrogen peroxide vapour process and again, CACR invites reasoned reactions.

Finally this issue has a report on the very successful Cleanroom Technology Conference 2018 and a book review of Bill Whyte's new book, which is an extremely useful compendium of his published papers over the last 16 years: Advances in Cleanroom Technology.

CACR is very proud to announce that during the last few months it has increased its partnership arrangements with member societies of the ICCCS. Members of the following societies are now able to read the e-version of CACR as an additional member benefit:

- BCW (Belgium)
- VCCN (Holland)
- ICS (Ireland),
- ASENMCO (Russia)
- R3Nordic (Scandinavia)
- S2C2 (Scotland)
- TTD (Turkey)
- IEST (USA)

I hope you enjoy CACR 35.

John Neiger

Pick of the points

It is commonly assumed that the air supply to a cleanroom will remove most of the airborne contamination from cleanrooms. However, it has been shown in this article that a substantial percentage of macroparticles and MCPs (microbe carrying particles) are not removed by air but deposited onto surfaces. See article by W Whyte and K Agricola on page 4.

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EDITOR
John Neiger
T: +44 (0)1494 882094
M: +44 (0)7967 572958
e: jneiger@johnwrite.co.uk

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Published by:
E C Pharma
Passfield Business Centre,
Lynchborough Road,
Passfield, Liphook, Hampshire
GU30 7SB, UK
T: +44 (0)1428 752222
F: +44 (0)1428 752223
e: publisher@euromedcommunications.com
www.euromedcommunications.com

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Comparison of the removal of macroparticles and MCPs in cleanrooms by surface deposition and mechanical ventilation

W Whyte[1], and K Agricola[2]

[1] School of Engineering, University of Glasgow, Glasgow G12 8QQ;
[2] Technology of Sense BV, Institutenweg 15, Enschede, 7521PH, the Netherlands.

Abstract

The removal of macroparticles (particles ≥5µm) and microbe-carrying particles (MCPs) from cleanroom air occurs by surface deposition or ventilation. In an operational ISO Class 8 cleanroom, small particles ≥0.3µm and ≥0.5µm are mostly removed by air (>99%). The size where half the particles are removed by deposition and half by mechanical ventilation is about ≥10µm, and 90% of particles are removed by deposition when the particle size is ≥40µm. Results were calculated for other ISO cleanroom classifications, and for particles ≥5µm the percentage deposited onto surfaces varied from about 11% to 37%. The percentage of MCPs removed by surface deposition in Grade B, C and D cleanrooms that are graded according to the EU Guidelines to Good Manufacturing Practice (2005), varied from 8% to 26%.

Introduction

Cleanrooms are used to manufacture products that are sensitive to particle and MCP contamination. To minimise contamination, cleanrooms are ventilated with a copious supply of particle-free air that dilutes and removes airborne contaminants and, therefore, minimises deposition of contamination onto vulnerable surfaces. However, it is not possible for all airborne contaminants to be removed by ventilation, and surface deposition occurs.

The mechanisms that cause deposition of airborne particles onto cleanroom surfaces have been investigated and reported[1]. A variety of mechanisms are involved, but for macroparticles (particles ≥5µm), the most important mechanism is gravitational deposition, with over 80% of particles ≥10µm being shown to deposit by that mechanism.[1] Use of this information and a survey of the scientific literature shows that gravitational settling is the main mechanism down to about 5µm, and an important one down to about 0.5µm.

The source of airborne MCPs in cleanrooms is almost exclusively from personnel, and microbes in the air are normally carried on skin and clothing detritus, with an average equivalent aerodynamic diameter of 12 µm.[2, 3] Because of their size, gravitational deposition is the main mechanism of surface deposition from air of MCPs.

In a sealed room with no ventilation, the removal of particles and MCPs from air must be entirely by surface deposition, and in a room built like a high-speed wind tunnel, most airborne contamination will be removed by air. In intermediate ventilation situations found in cleanrooms, some particles and MCPs will be removed by deposition and some by ventilation. However, information on the comparative importance of these two mechanisms is lacking, and is investigated and discussed in this article for particles greater than 5µm, as well as MCPs, with some addition information about particles less than 5µm.

Equivalent diameter of airborne particles

Naturally-occurring particles found in cleanroom air exist in a variety of sizes, shapes, and specific gravities, and these properties affect their deposition velocity through the air. When airborne particles are counted by an airborne particle counter, the actual size, shape and density of particles are not measured, but the amount of light scattered. This scattered light is used to determine the equivalent diameter of a polystyrene latex sphere that scatters the same amount of light as the particle being measured.

In other situations, airborne particles are measured in terms of the equivalent aerodynamic particle diameter, which is the diameter of a sphere with a specific gravity of 1000kg/m^3 that has the same aerodynamic properties i.e. gravitation settling and impaction, as the particle being considered. If the particle concentration and deposition rate of a given size of particle is measured in a cleanroom, the deposition velocity can be obtained. This method has been previously described[4] and used to obtain the deposition velocities of a range of cumulative sizes of particles considered in this article. Knowing the deposition velocity, the equivalent aerodynamic diameter can be calculated by the Stokes settling equation (Equation 1). The equivalent aerodynamic diameter can also be measured by instruments such as a cascade sampler, or time-of-flight sampler, these instruments being described by Hinds.[5]

The main source of particles and MCPs in a typical cleanroom is personnel, who disperse these from their skin and garments. The specific gravity of skin particles has been reported by Leider and Buncke[6] as 1100kg/m^3, and polyester, which is normally used in the construction of cleanroom garments, has a specific gravity of 1380kg/m^3; it is therefore reasonable to assume an average specific gravity of 1200kg/m^3 for airborne particles in cleanrooms.

Calculation of deposition velocity of discrete sizes of airborne particles by the Stokes settling equation

The deposition velocity of an equivalent aerodynamic diameter of a discrete size of particle that settles through air under the influence of gravity can be calculated. A comprehensive treatment of this subject

is given in Hinds' book[5], where the calculations are based on the Stokes equation, which is as follows.

Equation 1

$$v_D = \frac{\rho_p . g . d^2 . C_C}{18\eta}$$

Where:
v_D = the deposition velocity (m/s),
ρ_p = specific gravity of particle (kg/m^3),
g = acceleration due to gravity (9.81 m/s^2),
d = equivalent aerodynamic particle diameter (m),
C_C = Cunningham slip factor,
η = viscosity of air (1.18 x 10^{-5} kg/m.s).

Included in Equation 1 is the Cunningham slip factor, which should be used with particles that have a diameter less than about 1.5 µm, as the deposition velocity is affected by 'slip' at the surface of the particle. The Cunningham slip factor is calculated as follows:

$$C_C = 1 + \frac{2.52\lambda}{d}$$

where, λ = mean free path of 0.066 µm at 20°C and 1 atmosphere, and the units of d are given in micrometres.

When particles are larger than about 75µm, Equation 1 will overestimate the deposition velocity, and Equation 2 should be used.

Equation 2

$$v_D = \left(\frac{\eta}{\rho_a d_p}\right) \exp(-3.070 + 0.9935.J - 0.0178.J^2)$$

Where:
ρ_a = the density of air at 20ºC (1.2 kg/m^3),
J is calculated as follows:

$$J = \ln\left(\frac{4.\rho_p.\rho_a.d^3.g}{3\eta^2}\right)$$

The deposition velocities of a range of discrete sizes of particles can be calculated by the equations given above, and are given in the second column of Table 1.

Deposition velocity of cumulative sizes of particles

Concentrations of particles in air and surfaces are normally measured in cleanrooms cumulatively, to include all particles larger than the stated size. The deposition velocities of a range of cumulative sizes of particles have been determined by both experiment and theory in an ISO Class 8 cleanroom[4] and the results are given in Table 1.

Calculation of the removal of particles by deposition using the equivalent virtual air change rate method

A method that can be used to measure the removal of airborne particles by surface deposition uses the 'equivalent virtual air change rate'.[7] This gives the air change rate that produces the same reduction of airborne particle concentration as obtained by surface deposition. Using this approach, the removal of particles by surface deposition can be directly compared to the removal by mechanical ventilation.

It has been shown[7] that the equivalent virtual air change rate can be calculated by the following Equation 3.

Equation 3

$$N_E = \frac{v_D}{H}$$

Where:
N_E = the equivalent virtual air change rate,
H = the height of the room.

If the equivalent virtual air change rate is calculated by Equation 3, and the overall air change rate in the cleanroom is known, then the removal of particles by surface deposition can be calculated by Equation 4 as a percentage of the total number of particles removed by both deposition and ventilation.

Equation 4

$$\text{Surface deposition of total airborne contamination } (\%) = \frac{N_E}{N_E + N_V} .100$$

Where:
N_V = overall air change rate in a cleanroom.

Calculation of the removal of particles by deposition using time of decay

An alternative approach to calculating the percentage of particles removed by surface deposition is to calculate the time it takes for a given proportion of airborne particles to decay by surface deposition. This time can then be compared to the time it takes for the same proportion of particles to decay by mechanical ventilation.

Time of decay of airborne particles by surface deposition

In a cleanroom, the rate of change of the concentration of macroparticles over a short time interval by means of surface deposition is given by the following differential equation:

$$\frac{dC}{C} = \frac{v_D . dt}{H}$$

Where:
C = particle concentration,
v_D = deposition velocity of particles,
t= time,
H = height of room.

Table 1: Deposition velocities of particles

Equivalent aerodynamic particle diameter (µm)	Deposition velocity (cm/s) of particles with discrete diameters	Deposition velocity (cm/s) of particles with cumulative diameters
0.3	0.0005	0.003
0.5	0.0012	0.006
5	0.09	0.29
10	0.36	0.91
25	2.3	4.2
40	5.8	9.1
50	9.0	13
100	29	41

This equation can be integrated to give the following equations:

$$\frac{C}{C_0} = \exp\left(\frac{-v_D.t}{H}\right) \quad \text{or}$$

$$\frac{C_0}{C} = \exp\left(\frac{v_D.t}{H}\right)$$

Where:
C_0 = concentration at time zero,
C = concentration after time t.

By taking natural logs and rearranging the equation

$$t = \frac{H.\ln(\frac{C_0}{C})}{v_D}$$

Changing from natural to base 10 logs

$$t = \frac{2.3.H.\log_{10}(\frac{C_0}{C})}{v_D}$$

When 90% of the particles have deposited, C_0/C is equal to 10, and Equation 5 is obtained, and from this equation the resulting time of deposition (t_D) can be calculated.

Equation 5

$$t_D = \frac{2.3.H}{V_D}$$

Removal of airborne particles by mechanical ventilation

The removal of particles in a non-UDAF cleanroom by mechanical ventilation conforms to an exponential decay, and the decrease in concentration over time is calculated by the following equation.[7]

$$C = C_0.e^{-N_V.t}$$

Where:
C = concentration at time t,
C_0 = concentration at time zero,
N_V = number of air changes in cleanroom, owing to mechanical ventilation,
t = time.

Rearranging the equation, and taking natural log of both sides,

$$\ln\left(\frac{C}{C_0}\right) = -N_V.t \quad \text{or}$$

$$\ln\left(\frac{C_0}{C}\right) = N_V.t$$

Rearranging,

$$t = \frac{\ln(\frac{C_0}{C})}{N_V}$$

Changing from natural logs to base 10 logs,

$$t = \frac{2.3.\log_{10}(\frac{C_0}{C})}{N_V}$$

When 90% of the particles have been removed by ventilation, C_0/C is equal to 10, and Equation 6 is obtained, and from this equation the resulting time of removal by ventilation (t_V) can be calculated.

Equation 6

$$t_V = \frac{2.3}{N_V}$$

If the removal of 90% of particles by deposition is calculated by Equation 5, and the removal of 90% of particles by ventilation is calculated by Equation 6, the removal by surface deposition can be calculated by Equation 7 as a percentage of the total number of particles removed from the cleanroom air.

Equation 7

Percentage of particles removed by surface deposition

$$= \frac{t_D}{(t_V + t_D)}.100$$

Calculation of the removal of airborne particles by deposition using the equivalent virtual air change method

To calculate the equivalent virtual air change rate for different cumulative diameters of particles, the deposition velocity of particles settling through air is required. Table 1 gives the deposition velocities (cm/s) of a range of cumulative particles sizes that were previously obtained by experiments carried out in an ISO Class 8 operational cleanroom.[4] The cleanroom had a height of 2.7m, and an air change rate of about 13 per hour (0.0036/s). Using this information, the equivalent virtual air change rates for a range of cumulative sizes of particles are calculated, and the removal of airborne particles by deposition as a percentage of the total of particles removed are ascertained. The results are given in Table 2.

It can be seen in Table 2 that less than 1% of small particles of ≥0.3µm and ≥0.5µm are removed by surface deposition. However, approximately 50% of the particles ≥10µm are removed by surface deposition, and 90% are removed when the size is ≥40µm.

Table 2: Percentage of particles deposited in a cleanroom

Cumulative particle size (µm)	Deposition velocity (m/s) of cumulative particle size	Equivalent virtual air change rate/hour owing to surface deposition	Percentage of particles deposited in cleanroom with 13 air changes/hour
0.3	0.000028	0.04	0.3
0.5	0.000064	0.09	0.65
5	0.0029	4	23
10	0.0091	12	48
25	0.042	56	81
40	0.091	121	90
50	0.13	173	93
100	0.41	547	98

Table 3: Percentage of different sizes of particles deposited in a cleanroom

Cumulative particle size (µm)	Number of seconds to decay to 90% of airborne concentration owing t o surface deposition	Number of seconds to decay to 90% of airborne concentration owing to mechanical ventilation	Percentage of particles deposited in cleanroom
0.3	222075	638	0.29
0.5	97158	638	0.65
5	2144	638	23
10	683	638	48
25	148	638	81
40	68	638	90
50	48	638	93
100	15	638	98

Calculation of the removal of airborne particles by deposition using the decay method

To calculate the percentage of airborne particles deposited by the time of decay method, deposition velocities (m/s) are required. These are given in Table 1 for an ISO Class 8 cleanroom in operation, which has a height of 2.7m and 13 air changes per hour (0.0036/s). The number of seconds for the airborne particles to decay to 90% of their concentration by surface deposition was calculated by means of Equation 5, and the number of seconds to decay to 90% of their airborne concentration by mechanical ventilation was calculated by Equation 6; both sets of results are given in Table 3. The percentage of deposited particles of the total removed by both surface deposition and ventilation was then calculated by means of Equation 7, and the results given in Table 3. It can be seen that these percentages are identical to those reported in the previous section, where the results were calculated by the equivalent air change method.

Surface deposition of particles ≥5µm with respect to airborne cleanliness

The results calculated in the previous two sections are based on deposition velocities that were obtained from experiments carried out in an ISO Class 8 cleanroom.[4] In cleaner cleanrooms with a greater air change rate, a higher percentage of particles may be removed by ventilation. However, it is also known that higher air supply rates are associated with higher deposition velocities of particles,[4, 8] which may partly balance their greater removal by ventilation. This possibility was investigated.

The rate that particles deposit onto cleanroom surfaces is determined by the particle deposition rate (PDR), which is the rate of deposition of particles onto a standard surface area e.g. 1 m^2, in a standard time e.g. 1 hour. The PDR is measured by exposing a witness plate, or collection surface of an instrument, and the number of particles of a specified size that deposit onto the collection surface in a given time is obtained, and then the PDR. In cleanrooms, it is the cumulative number of particles of different sizes that are usually measured.

It has been reported by Hamburg[8] that the PDR of particles ≥5µm onto cleanroom surfaces varies, with a higher deposition rate in cleaner rooms. Cleanrooms that ranged in airborne cleanliness from ISO Class 5 to ISO Class 9 were studied, and the following relationship (modified to SI units) reported. A similar relationship has also been reported by Parasuraman et al.[9] The relationship reported by Hamburg, when converted to metric units, is as follows.

$$PDR \geq 5\mu m = 0.0226.C_{\geq 5\mu m}{}^{0.773}$$

Where:
$PDR_{\geq 5\mu m}$ = deposition rate of particles ≥5µm/m^2/s,
$C_{\geq 5\mu m}$ = airborne concentration per m^3 of particles ≥5µm

However, it is known[4] that

Equation 8

$$\mathrm{PDR} = C_D.v_D$$

Where:
C_D = airborne concentration per m^3 of particles of cumulative size of D µm, and
v_D = deposition velocity (m/s) of particle diameter, D.

Therefore,

Equation 9

$$v_{\geq 5\mu m} = \frac{0.0226.C_{\geq 5\mu m}{}^{0.773}}{C_{\geq 5\mu m}} = 0.0226.C_{\geq 5\mu m}{}^{-0.227}$$

ISO 14644-1[10] cleanrooms of Class 5, and cleaner, have low concentrations of particles ≥5µm and, therefore, these particles are not used to specify class limits. Also, the low particle concentrations in ISO Class 5 and cleaner cleanrooms are unlikely to be achieved by non-unidirectional airflow systems, but by means of the more effective unidirectional airflow system. However, the calculation of the percentage deposition in this article uses air change rates and, therefore, calculations of the percentage of surface deposition can only be carried out in ISO classes 6 to 9.

The deposition velocities of particles ≥5µm in ISO Classes 6 to 9 in the operational state are calculated by Equation 9 and given in Table 4. Also given in Table 4 is the PDR limit for this range of cleanrooms, as calculated by Equation 8. Using a ceiling height of 2.7m, the equivalent virtual air change rate owing to deposition is calculated by use of Equation 3, and the results given in Table 4.

Table 4: Percentage of particles ≥5µm removed by deposition in a range of ISO cleanroom classes

ISO Class	6	7	8	9
Class limit (no./m³) for particles ≥5µm	293	2930	29300	293000
Deposition velocity (m/s)	0.00623	0.00369	0.00219	0.00130
PDR limit of particles ≥5µm per m² per hour	6566	38931	230834	1368673
Equivalent virtual air change rate/hour owing to surface deposition	8.3	4.9	2.9	1.7
Typical air changes/ hour	30 to 70	20 to 40	5 to 15	5
Particles removed by surface deposition (%)	22 to 11	20 to 11	37 to 16	26

To calculate the proportion of airborne particles removed by surface deposition as a percentage of the total removed by both deposition and ventilation, it is necessary to know the air change rates needed to achieve the ISO class of cleanroom being studied. Unfortunately, it is not possible to use an exact air change rate. There are two main reasons for this. Firstly, the air cleanliness of a cleanroom is determined by the air supply rate and not by the air change rate,[7] and for the same ISO class limit of particle concentration, the smaller the cleanroom, the greater the air change rate required. Secondly, the airborne cleanliness of a cleanroom is directly related to contamination dispersed into the air by personnel and other sources of contamination. This will vary between cleanrooms and, therefore, so will the air change rate required for a given ISO Class of cleanroom. Taking these reasons into consideration, a range of air change rates for each ISO class are given in Table 4 that the authors considered to be typical of those found in cleanrooms. Using these air change rates, the percentage of particles ≥5µm removed by surface deposition can be calculated by use of Equation 7, and the results are given in Table 4.

Percentage of MCPs removed by deposition

Shown in Table 5 is the airborne concentration of MCPs given in the EU Guidelines to Good Manufacturing Practice (EU GGMP): 2008[11] for Grade B, C and D cleanrooms. Grade A clean zones are not included in the table as these normally use unidirectional airflow and, therefore, cannot be analysed by the method used in this article. Also shown in Table 5 are the ISO 14644-1 classes that correspond to the EU GGMP grades in the operational state.

Micro-organisms are not usually found in cleanroom air as unicellular organisms, as they are dispersed by personnel on skin and clothing detritus, and known as microbe-carrying particles (MCPs), with an average equivalent aerodynamic diameter of about 12 µm.[2,3]

It has been reported[12] that the deposition velocities of airborne MCPs increase with airborne cleanliness in a similar manner to particles, as discussed in the previous section. The deposition velocity of MCPs can be calculated by the following equation given in the referenced article.[12]

Equation 10

$$v_{D:MCPs} = 0.0161.C^{0.6571}$$

Where:
$v_{D:MCPs}$ = deposition velocity of MCPs (m/s),
C = concentration of airborne MCPs /m³.

Shown in Table 5 are the average deposition velocities calculated by Equation 10 using the concentrations of MCPs expected in Grade B, C and D cleanrooms. Also shown in Table 5 are the equivalent virtual air change rates caused by surface deposition as calculated by Equation 3, when the ceiling height is 2.7 m. To obtain the surface deposition as a percentage of the total amount removed by both deposition and ventilation, the air change rate is required for the three grades of cleanrooms, and a range of air changes that are typical of pharmaceutical cleanrooms are given in Table 5. It can be seen that the air change rate is higher than given in Table 4 for similar ISO classes, this being partly owing to the greater need for a higher air supply to achieve the required concentration of MCPs.[13] Finally, in the last column of Table 5 is the percentage of airborne MCPs removed by surface deposition as a percentage of the total removal by both deposition and ventilation. It can be seen that in a typical EU GGMP Grade B cleanroom, surface deposition of MCPs will remove about 9% to 24% of the airborne MCPs. In a Grade C cleanroom it will be 8% to 18%, and in a Grade D it will be 10% to 26%.

Discussion and conclusions

Particles and microbe-carrying particles (MCPs) in cleanroom air are removed by means of mechanical ventilation or by surface deposition, and this article provides information about the relative importance of these two removal mechanisms. The importance of surface deposition is expressed as the percentage of particles deposited of the total number of particles removed by both deposition and ventilation.

The percentages of a cumulative range of particles sizes removed by surface deposition were calculated from the deposition velocity of a cumulative range of particle sizes obtained in an operational ISO Class 8 cleanroom.[4] The calculation of percentage deposition was carried out using two different approaches. The first approach was to calculate the particles deposited onto surfaces in terms of equivalent virtual air change, which is the air change rate that produces the same reduction in airborne particles as obtained by surface deposition. The equivalent virtual air change rate was then compared with the actual air change rate owing to mechanical ventilation. The second approach was to calculate the time for

Table 5: Percentage of surface deposition in different grades of airborne microbial cleanliness

EU GGMP cleanroom grade	ISO Class (operational)	Upper limit of airborne MCP concentration/ m^3	Deposition velocity of MCPs (m/s)	Equivalent virtual air changes per hour	Typical range of air changes per hour	Surface deposition (%)
Grade B	7	10	0.0073	9.7	30-100	24% to 9%
Grade C	8	100	0.0033	4.4	20-50	18% to 8%
Grade D	Not defined	200	0.0026	3.5	10-30	26% to 10%

airborne particles to decay by both deposition and ventilation to 90% of their concentration. The number of particles deposited was then calculated as a percentage of the total number of particles removed by both deposition and ventilation.

The results of the two types of calculations are given in Tables 2 and 3, where it can be seen that they give identical results and, therefore, give confidence in the correctness of the overall analytical approach. For cumulative particles sizes of ≥0.3µm, ≥0.5µm, ≥5µm, ≥10µm, ≥25µm, ≥40µm, ≥50µm, and ≥100µm, the percentage removed by surface deposition was 0.3%, 0.65%, 23%, 48%, 81%, 90%, 93% and 98%, respectively. It can, therefore, be seen that (a) smaller particles of ≥0.3µm and ≥0.5µm are mostly removed by ventilation (b) the size where 50% of the particles are removed by deposition is close to ≥10µm and (c) about 90% of the particles are deposited at a size of ≥40µm.

In sealed and unventilated rooms, all particles will be removed from the air by surface deposition, but in a room designed like a high-speed wind tunnel, most particles would be removed by ventilation. Cleanrooms will take some intermediate position, where some particles are removed by deposition and some by ventilation.

The results reported in the previous paragraphs were calculated from information previously reported from experiments carried out in an operational ISO Class 8 cleanroom.[4] However, it would be expected in cleaner rooms with higher air supply rates that the removal of particles by ventilation would be higher, and the removal by surface deposition, lower. However, it is also known that as the airborne cleanliness improves and the air supply increases, the deposition velocity of particles increases, and more surface deposition occurs.[4, 8] The effect of these two mechanisms may balance each other and a change in the percentage deposited may not be as much as speculated. This possibility was investigated.

Using information available on the relationship of particle deposition rate and air cleanliness for particles ≥5µm,[4, 8] the percentages of surface deposition were calculated for cleanrooms that ranged from ISO Class 6 to ISO Class 9, and the results given in Table 4. However, to calculate the deposition percentage over a range of ISO classes, it is necessary to make assumptions as to what air change rates are associated with what cleanliness classes. Because of the reasons given, the air change rates needed to obtain a required ISO class will vary. Therefore, a range of air changes that are typical of each ISO class was used, and the calculated percentage deposited also given as a range. These results show that the deposition percentage of particles ≥5µm varied from about 11% to 37% across cleanroom classes of 6 to 9, with a tendency for a higher deposition percentage to be associated with poorer cleanliness classes. However, this tendency was not clear, but until further experimental results are available, the results of percentage deposition that apply to an ISO Class 8 can be applied to ISO Classes 6, 7 and 9.

An investigation was also carried out to ascertain the percentage deposition of MCPs in cleanrooms. Microbes are not normally found in cleanroom air in unicellular form, as they are dispersed by personnel on skin and clothing detritus, and have an average equivalent aerodynamic size of about 12µm.[2, 3] Similar to particles, the deposition velocity of MCPs is known to increase with the cleanliness of the cleanroom[12] and, using the calculated deposition velocities, the deposition percentages of MCPs in EU GGMP (2008) Grades B to D cleanrooms were calculated. These percentages were based on a range of typical air change rates found in these grades of cleanrooms, and the percentage varied from about 9% to 26%. Similar to the results with particles ≥5µm, the percentage of deposition does not appear to be significantly affected by the grade of cleanroom.

It is commonly assumed that the air supply to a cleanroom will remove most of the airborne contamination from cleanrooms. However, it has been shown in this article that a substantial percentage of macroparticles and MCPs are not removed by air but deposited onto surfaces. The percentage deposited varies according to particle size and the amount of mechanical ventilation required to achieve a specific standard of air cleanliness. The importance of surface deposition shows that when the control of airborne contamination of surfaces is being considered, more thought should be given to monitoring of the PDR,[14] and consideration of activities such as walking and touching of surfaces that will cause deposited macroparticles and MCPs to re-enter the cleanroom air, and subsequently deposit onto vulnerable surfaces. Effective control of such contamination cannot be achieved solely by mechanical ventilation and attention must be given to efficient

and frequent cleaning of surfaces.

References

1. Whyte W, Agricola K and Derks M. Airborne particle deposition in cleanrooms: deposition mechanisms. *Clean Air and Containment Review* 2015; Issue **24**: 4-9. Available at http://eprints.gla.ac.uk/111678/1/111678.pdf
2. Noble WC, Lidwell OM and Kingston D. The size distribution of airborne particles carrying micro-organisms. *Journal of Hygiene* 1963; **61**:385-391.
3. Whyte W and Hejab M. Particle and microbial airborne dispersion from people. *European Journal of Parenteral and Pharmaceutical Sciences* 2007; **12**(2): 39-46. Available at http://eprints.gla.ac.uk/84357/1/84357.pdf
4. Whyte W, Agricola K and Derks M. Airborne particle deposition in cleanrooms: relationship between deposition rate and airborne concentration. *Clean Air and Containment Review* 2016; Issue **25**: 4-10. Available at http://eprints.gla.ac.uk/119091/1/119091.pdf
5. Hinds WC. Aerosol technology: properties, behaviour and measurement of airborne particles. –Second Edition 1999. Wiley-Interscience, ISBN 0-471-19410-7.
6. Leider M and Buncke CM (1954). Physical dimensions of the skin. *AMA Archives of Dematology and Syphilology*; **69**: pp563-569.
7. Whyte W, Whyte WM and Eaton T. The application of the ventilation equations to cleanrooms Part 1: The equations. *Clean Air and Containment Review* 2012; Issue **12**: 4-8. Available at http://eprints.gla.ac.uk/84186/1/84186.pdf
8. Hamberg O. Particle fallout predictions for clean rooms. *The Journal of Environmental Sciences* 1982; **25**: 15-20.
9. Parasuraman DK, Kemps AAM, Veeke HPM and Lodewijks G. Prediction model for particle fallout in cleanrooms. *Journal of the IEST* 2012; **55**(1): 1-9.
10. ISO 14644-1 (2015). Cleanrooms and Associated Controlled Environments –Part 1: Classification of air cleanliness by particle concentration. International Organization for Standardization, Geneva, Switzerland.
11. EU GGMP (2008). The rules governing medicinal products in the European Union –Volume 4 -EU guidelines to good manufacturing practice – medicinal products for human and veterinary use – Annex 1 –Manufacture of sterile medicinal products. European Commission, Brussels.
12. Whyte W and Eaton T. Deposition velocities of airborne microbe-carrying particles. *European Journal of Parenteral and Pharmaceutical Sciences* 2016; **21**(2): 45-49. Available at http://eprints.gla.ac.uk/121686/1/121686.pdf
13. W Whyte, T Eaton, WM Whyte, N Lenegan, S Ward and K Agricola. Calculation of air supply rates and concentrations of airborne contamination in non-UDAF cleanrooms. *European Journal of Parenteral and Pharmaceutical Sciences* 2017; **22**(2): 38-49. Available at http://eprints.gla.ac.uk/147757/1/147757.pdf
14. Agricola K. Practical experiences in particle deposition monitoring. *Clean Air and Containment Review* 2015; Issue **21**: 4-8.

W (Bill) Whyte, B.Sc. (microbiology), D.Sc. (mechanical engineering) and Honorary Research Fellow at Glasgow University, has been involved with cleanrooms for over 50 years. He has published over 140 reports and papers and written three major books on the subject, the latest of which, *Advances in Cleanroom Technology*, has just been published – see review on page 20. He is a founder and former chairman of the Scottish Society for Contamination Control and the Cleanroom Testing and Certification Board - International. He is a member of the BSI committee involved in the writing of cleanroom standards. He has extensive experience as an industrial consultant and running cleanroom courses.

Koos Agricola is an Applied Physicist and has worked in R & D at Océ Technologies, a Canon Company, since 1986 and part time at Technology of Sense since 2017. His responsibilities include contamination control in cleanrooms for the manufacture of critical parts. Koos is a member of ISO/TC 209, convenor of WG 14, secretary of WG 4 and technical expert in ISO/TC 209 WGs 3, 11, 12 and 13 as well as CEN/TC 243 WG 5. He is chairman of the ICCCS Education and Technical Committees and the CTCB-I and secretary of the VCCN and the ISCC 2018 steering committee.

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Getting rid of 95% UCL calculations in ISO 14644-1:2015 standard: new weaknesses and possible solutions

Alexander Fedotov

Abstract

Cleanroom testing and classification are considered by all parties involved in cleanrooms design, construction, testing and operation. There is a rather long history, but some unsolved problems still remained at the beginning of the 21st century. One of the problems was the unnecessarily complicated procedure of 95% UCL calculations using statistical tools. Field engineers were keen to abandon these calculations without losing any information. It is quite possible to do this by increasing the number of sampling points or setting lower concentrations for the class limits in the testing procedures. The new ISO 14644-1:2015 made a step forward and offered a much simpler method by allowing the use of single measurements or mean values simply by increasing the number of sampling locations. This paper discusses the pro and cons of this approach and offers alternative suggestions.

General

ISO 14644-1:2015 *Cleanrooms and associated controlled environments – Part 1: Classification of air cleanliness by particle concentration* is a revision of ISO 14644-1:1999. One of the reasons for the revision was because the 1999 version had a disadvantage in that it required calculation of the 95 % Upper Confidence Level (95% UCL) where the number of sampling locations N_L lay between two and nine ($2 \leq N_L \leq 9$). This procedure is laborious on a routine basis and field technicians wanted to get rid of it.

Getting rid of the 95% UCL

ISO 14644-1:1999 specified the minimum number of sampling locations N_L by the widely used square root rule:

$N_L = \sqrt{A}$ with rounding up to the next integer value, where A is the area of cleanroom in m^2.

Calculation of 95 % UCL was only required if $2 \leq N_L \leq 9$. If $N_L = 1$ or $N_L \geq 10$ only particle concentrations (single or average) were required and computing of 95 % UCL was not applicable.

UCL is needed to reflect the statistical nature of a process/event and to estimate random error. This error can be reduced by increasing the number of sampling locations to $N_L \geq 10$ or more. ISO 14644-1:1999 says that for $N_L \geq 10$ the statistical error can be neglected. No objections to this were noted.

However, increasing N_L to 10 is not always practical because the sampling can be excessive, say when $N_L = 5$ according to a square root rule. Therefore it is was attractive to get rid of the UCL calculation for $2 \leq N_L \leq 9$. This is possible in two different ways:

- by increasing number of sampling locations;
- by setting lower limits for concentrations depending on number of sampling locations.

One should remember that getting rid of 95 % UCL requires an increase in sampling locations or lower concentration limits. It is not possible to abandon UCL and at the same time to decrease the

Table A.1 of ISO 14644-1:2015 – Sampling locations related to cleanroom area

Area of cleanroom (m^2) less than or equal to	Minimum number of sampling locations to be tested (N_L)
2	1
4	2
6	3
8	4
10	5
24	6
28	7
32	8
36	9
52	10
56	11
64	12
68	13
72	14
76	15
104	16
108	17
116	18
148	19
156	20
192	21
232	22
276	23
352	24
436	25
636	26
1 000	27
>1 000	See Formula (A.1) in standard

number of sampling locations or to set looser conditions. This is an important starting point in order to understand what has happened.

The new method in ISO 14644-1:2015

ISO 14644-1:2015 cancelled the square root rule for determining the number of sampling locations N_L.

Table A.1 of ISO 14644-1:2015 defines N_L for a range of cleanroom areas.

The new standard simplifies cleanroom testing for numbers of sampling locations $2 \leq N_L \leq 9$ but is it correct?

Table A.1 is based on two assumptions:

- the adaptation of the hypergeometric sampling model technique provides the necessary statistical confidence;
- the area immediately surrounding each sampling location has a homogeneous particle concentration.

It is the author's opinion that both assumptions challenge reality, do not reflect the nature of cleanrooms and can be less precise than the Normal statistical model in ISO 14644-1:1999.

The hypergeometric distribution is a standard model where samples are drawn randomly without replacement from a finite population. It is widely used for testing materials and products, but it is not, in the author's opinion, suitable for cleanrooms. In the 1970s and 80s, the author of this paper investigated how the results of statistical exercises depend on the distribution model applied (normal, log-normal, Poisson etc.) and found that results can differ by an order of magnitude for the same task! So the selection of the distribution model is critical and an arbitrary approach without a scientific rationale is not acceptable.

Distribution models for random values are very specific. Dedicated knowledge and experience are essential for selecting the right model.

The same applies to the assumption on local homogeneity of the particle concentration. Local can mean an area of more than 10 m². According to Table A.1, the number of sampling locations for a cleanroom with an area of 232 m² will be $N_L = 22$ and the local area will be 10.5 m². Particle concentration will never be homogeneous in such a large area!

Table 1: Comparison of minimum numbers of sampling location in the two standards

Area A of cleanroom (m²) less than or equal to	Minimum number of sampling locations N_L in		Decreasing (–) or increasing (+) of N_L in ISO 14644-1:2015 vs ISO 14644-1:1999	
	Table A.1 of ISO 14644-1:2015	ISO 14644-1:1999, $N_L = \sqrt{A}$	Numbers	%
2	1	2	–1	–100 %
4	2	2	0	0
6	3	3	0	0
8	4	3	+1	+33 %
10	5	4	+1	+25 %
24	6	5	+1	+20 %
28	7	6	+1	+17 %
32	8	6	+2	+33 %
36	9	6	+3	+50 %
52	10	8	+2	+25 %
56	11	8	+3	+38 %
64	12	8	+4	+50 %
68	13	9	+4	+44 %
72	14	9	+5	+56 %
76	15	9	+6	+67 %
104	16	11	+5	+45 %
108	17	11	+6	+55 %
116	18	11	+7	+64 %
148	19	13	+6	+46 %
156	20	13	+7	+54 %
192	21	13	+8	+62 %
232	22	16	+6	+38 %
276	23	17	+6	+35 %
352	24	18	+6	+33 %
436	25	21	+4	+19 %
636	26	26	0	0
1 000	27	31	–4	–13 %

An analogy would be to approximate the Alps with cubes and to construct bridges and tunnels on that basis.

In fact the hypergeometric sampling model technique, where samples are drawn randomly without replacement from a finite population, and the assumption that the area immediately surrounding each sampling location has a homogeneous particle concentration mean that two different distributions (hypergeometric and homogeneous) are used in the same model! The random factor is not appropriate in a homogeneous distribution.

Consequences of the new method

ISO 14644-1:2015 sets much less rigorous conditions than the existing standard for small cleanrooms.

It also gives an increasing number of sampling locations with increasing cleanroom area for 6 < A ≤ 76 m². This contradicts the fundamental rule of statistics that the more information available, the more can be the confidence and the less the density of sampling locations!

Even more confusion is observed for bigger cleanrooms with areas 81 < A ≤ 625 m². The old standard does not require UCL for areas A > 81 m² ($N_L \geq 10$). The new standard requires more sampling locations (from 30 to 64 % for this case). This means unnecessary extra costs.

ISO 14644-1:2015 thus sets more complicated and expensive procedures for some cases without any positive benefits and has serious consequences. Table 1 compares the number of sampling locations according to ISO 14644-1:1999 with the number of sampling locations from Table A.1 of ISO 14644-1:2015 to illustrate what has happened.

This Table can be separated into four distinct parts:

1. Cleanroom areas 1 < A ≤ 6 m²

For cleanroom area A = 2 m² the old standard specifies the number of sampling locations $N_L = \sqrt{A} = 1.41 \approx 2$ (rounding up to bigger value). This falls into $2 \leq N_L \leq 9$ and calculation of 95 % UCL is required.

Table 1 of ISO 14644-1:2015 shows that $N_L = 1$ for this area and no UCL calculation is needed.

For A = 4 m² and A = 6 m², the number of sampling locations for both the 1999 and the 2015 standards is the same. So for the smallest areas, ISO 14644-1:2015 sets less rigorous conditions than ISO 14644-1:1999. Such areas are often used for the most critical operations, e.g. in the aseptic core. If UCL calculations for $2 \leq N_L \leq 9$ are abandoned, the number of sampling locations should be increased, not decreased or at least kept at the same level.

2. Cleanroom areas 6 < A ≤ 76 m²

An interesting picture can be be observed here. For A = 8 m² ISO 14644-1:2015 specifies $N_L = 4$ sampling locations but ISO 14644-1:1999 specifies 3 sampling locations, so the number of sampling locations in the 2015 standard is 33 % more than in the 1999 standard. For an area A = 76 m² the sampling locations are 15 and 9 respectively, an increase of 67 %. So the difference between the new standard and the old standard increases as the size of the cleanroom area increases. The author questions whether there is any evidence that the old standard was inadequate in this range to justify these increases.

3. Cleanroom areas 76 < A ≤ 625 m²

ISO 14644-1:1999 does not consider statistical deviations and so does not require the calculation of UCL for areas A > 81 m², $N_L \geq 10$. (76 m² is not far from 81 m² so the difference between 76 and 81 can be ignored for simplicity). ISO 14644-1:1999 has been well accepted in practice over many years and there is no evidence that the method needed to be changed, but it was. The unnecessary increase in numbers of sampling locations of between 30 and 64 % in the new standard, means an unnecessary increase in time and costs for cleanroom testing. Why have more sampling locations than before for these larger areas, when the confidence for the smaller areas has been decreased? Surely this is not scientific.

Table 2: Numbers of sampling locations with safety margin

A, m²	N_L	Correction factor/safety margin %
A ≤ 1	1	
1 < A ≤ 2	3	up to 150 %
2 < A ≤ 4	4	up to 100 %
4 < A ≤ 9	4	up to 90 %
9 < A ≤ 16	5	up to 60 %
16 < A ≤ 25	6	up to 50 %
25 < A ≤ 36	7	up to 40 %
36 < A ≤ 49	8	up to 30 %
49 < A ≤ 64	9	up to 25 %
64 < A ≤ 81	10	up to 10%
A > 81	√A ≥ 10	0

Table 3: Numbers of sampling locations according to square root rule with safety margin for particle concentration

A, m²	$N_L = \sqrt{A}$	Safety margin: suggested % of maximum allowable particle concentration
A ≤ 1	1	
1 < A ≤ 2	2	45 %
2 < A ≤ 4	2	50 %
4 < A ≤ 9	3	55 %
9 < A ≤ 16	4	60 %
16 < A ≤ 25	5	65 %
25 < A ≤ 36	6	70 %
36 < A ≤ 49	7	75 %
49 < A ≤ 64	8	80 %
64 < A ≤ 81	9	90 %
A > 81	10	100%

4. Cleanroom areas A > 625 m²
For A = 636 m² both old and new standards give the same number of sampling locations, i.e. 26.

However, the next and final step to 1000 m² requires an additional 4 sampling locations. This is also not scientific.

Other methods of getting rid of UCL calculations

Two methods can be proposed.

1. Increasing the number of sampling locations where 2 ≤ N ≤ 9 by using the square root rule with a correcting factor or safety margin according to Table 2.
2. An alternative but essentially similar approach would be to specify tighter concentration limits without increasing the number of sampling locations per the square root rule. This is shown in Table 3.

The safety margin reduces as the number of sampling locations N_L increases and the % becomes 100 for $N_L \geq 10$. The percentages can be adjusted but the idea reflects the statistical nature of particle concentration.

Conclusion

The problems with the old and new sampling methods and the availability of possible alternatives suggest that the best way forward would be for the experts to agree and arrange to carry out a series of studies of sampling in cleanrooms with the object of determining which sampling method is best.

Dr. Alexander E. Fedotov has more than 40 years' experience of work in research and industry. His primary speciality is automatic control systems. For the last 30 years he has been involved in cleanrooms, latterly in GMP areas. He is Managing Director of Clean Technologies LLC, a private company based in Moscow, Russia. The company is active in cleanroom design and testing for different areas of application, especially for the pharmaceutical industry and hospitals. Dr. Fedotov was one of the founders of the Russian Association of Engineers for Contamination Control (ASENMCO) in 1991. He is currently President of ASENMCO and editor of the magazine *Technology of Cleanliness* in Russian. He is also the editor of three books: *Cleanrooms* in 1998; 2003 and 2015, *Basics of GMP* in 2012 and *Manufacturing Sterile Medicinal Products* in 2012 (all three in Russian) and has contributed two chapters to *Cleanroom Management in Pharmaceuticals and Healthcare* (Euromed), 2012 in English. He is Chairman of the Russian Technical Committee for standardization TC 184:Industrial cleanliness, and Russian delegate to several working groups of ISO TC 209: Cleanrooms and associated controlled environments. e-mail: fedotov@invar-project.ru web: www.invar-project.ru

Removal of airborne contamination using hydrogen peroxide vapour (HPV)

Shada Warreth[1], Michael Wood[2], and John Chewins[3*]

[1] National Institute for Bioprocessing, Research & Training, Co. Dublin, Ireland; [2] Bioquell Ireland, Limerick, Ireland; [3] Bioquell UK, Andover, UK; *. Corresponding author

Abstract

Hydrogen peroxide vapour is an established method for removing microbiological contamination from surfaces. Whilst surface decontamination is well studied, the effect of vapour phase hydrogen peroxide on microbiological organisms within the air has not been well evaluated, with decontamination efficacy being generally assumed. Active viable monitoring of an ISO Class 7 / Grade B simulated cleanroom pre and post hydrogen peroxide vapour decontamination showed the elimination of all microbiological organisms from the air.

Keywords

Hydrogen peroxide, cleanroom, air sampling, decontamination

Introduction

Hydrogen peroxide vapour (HPV) is a biocidal agent used for the disinfection and sterilisation of surfaces. Over the past two decades, environmental biodecontamination of hospitals, cleanrooms, isolators, etc. using 30-35% hydrogen peroxide vapour has become established. Formaldehyde has historically been the accepted method of enclosure surface decontamination, but its classification as a human carcinogen (Category 1B) is driving users and regulators to find safer alternatives and increasing the use of HPV.[1]

Hydrogen peroxide vapour biodecontamination is a microcondensation-based process.[2, 3] HPV is introduced into an enclosure, saturating the air. At the point of saturation, known as the dew-point, the air can no longer support the introduction of additional vapour and therefore hydrogen peroxide is laid down onto the surfaces as an invisible microcondensation.[4] The formation of microcondensation on surfaces, and the microbiological organisms residing on those surfaces, has been studied and visually recorded.[5] However, microorganisms within an enclosure are not only present on surfaces, but also within the air. Shimose et al.[6] indicate air to be a route of transmission for nosocomial pathogens within the hospital environment. Fomites within the air should be exposed to the same microcondensing conditions as other surfaces within the enclosure, thus microbiological organisms should be eliminated from the air as well as surfaces. Taneja[7] carried out a study using an aerosol fogging hydrogen peroxide system, with settle plates placed within the enclosure to determine air disinfection. Aerosol fogging systems disperse a liquid biocide and do not employ the HPV-based microcondensation mechanism, thus the study by Taneja may not be representative of an HPV system.

The Irish National Institute for Bioprocessing, Research and Training (NIBRT) was asked to carry out a study to confirm the surface disinfection efficacy of 35% hydrogen peroxide vapour throughout a cleanroom, including the air.

Materials and methods

A hydrogen peroxide vapour system (Bioquell Ireland, Limerick, Ireland) consisting of three hydrogen peroxide vapourisation modules and four aeration units was located in a simulated Grade B / ISO Class 7 , 250m^3 pharmaceutical fill/finish cleanroom. 35% Hydrogen Peroxide (HPV-AQ, Bioquell UK, Hampshire, UK) compliant with the requirements of the Irish Pesticide Registration and Controls Division (PCS number 97584) was obtained and placed into the generators. All HVAC ducts were sealed, along with all entry and exit doors, apart from a single entry/exit door. Six biological indicators containing >1 x 10^6 endospores of *Geobacillus stearothermophilus* (Bioquell UK, Hampshire, UK) were located on surfaces throughout the cleanroom by an independent microbiologist. Surfaces included challenging locations such as behind and underneath isolator and RABS equipment. Two additional biological indicators were retained as positive controls.

A portable active air sampler (EMD Millipore M Air T™, Merck Millipore, Watford, UK) containing a Tryptone Soya Agar (TSA) plate (Millipore M Ait T cassette, Merck Millipore, Watford, UK) was placed into the centre of the cleanroom, by an operator wearing Grade B sterile garments. A standard air sampling cycle was performed in accordance with the M Air T user guide, wherein 1m^3 of air was moved through the device over a period of seven minutes. The plate was incubated at 20-25°C for 7 days, followed by 30-35°C for a further 7 days.

The cleanroom's remaining entry / exit was sealed and the hydrogen peroxide decontamination cycle initiated. The system injected hydrogen peroxide for 20 minutes and then allowed the hydrogen peroxide to contact or dwell on the surfaces for a further 25 minutes. This was followed by aeration to ≥ 1.0ppm measured using a calibrated hand held monitor (Draeger, Plymouth, UK).

The cleanroom was re-entered by a Grade B garmented operator and the active air sampling process repeated. The operator remained in the room in a stationary position during the sampling. On completion of the sampling cycle, the biological indicators were transferred into 10ml tubes of Tryptone Soya Broth (TSB) (Biomerieux, Basingstoke, UK). The air sampling plate was incubated as previously described and the TSB tubes, including the two BIs retained as positive controls, were incubated at 57.5°C (±4.5°C) for 7 days.

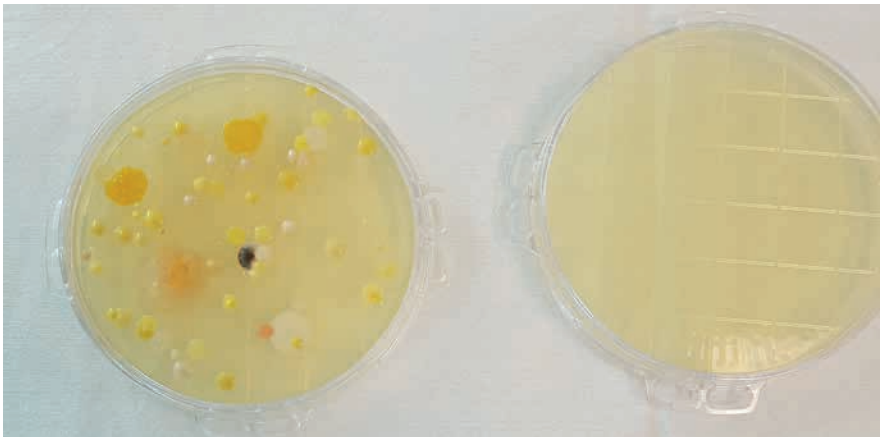

Figure 1: Active air sampling plates pre (left) and post (right) HPV biodecontamination after incubation.

Results

The biological indicators within the TSB all exhibited zero growth (<1 cfu) after 7 days incubation, apart from the two positive control tubes, which showed copious growth (turbid solution). This indicates that a 6 log sporicidal kill was achieved at all challenge locations.

The active air sampling prior to the hydrogen peroxide decontamination identified 67 cfu/m^3 and the active air sampling post HPV application showed no visible growth (<1 CFU/m^3). See Figure 1.

Discussion

The results of the study add further support to the established body of scientific evidence showing hydrogen peroxide vapour to be an effective surface biodecontamination agent, and importantly also demonstrate that 35% hydrogen peroxide vapour is able to eliminate microbiological organisms present within the air providing an aseptic enclosure.

The study is limited due to the fact that a single decontamination run was performed and a single air sample, pre and post HPV application was obtained.

Conclusion

35% hydrogen peroxide vapour was shown to achieve a 6 log sporicidal reduction on cleanroom surfaces in challenging locations and eliminate microbiological contamination from within the air.

Conflicts of Interest

S. Warreth has no conflict of interest to declare

J.Chewins and M.Wood are employees of Bioquell, a manufacturer of hydrogen peroxide vapour biodecontamination systems.

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References

1. UK Health and Safety Executive. Formaldehyde. https://webcommunities.hse.gov.uk/connect.ti/microbiologicalhazards/view?objectId=238224&exp=e1. Accessed 20 Dec 17.
2. Unger-Bimczok, B., Kottke, V., Hertel, C., and Rauschnabel, J. (2008). The influence of humidity, hydrogen peroxide concentration, and condensation on the inactivation of Geobacillus stearothermophilus spores with hydrogen peroxide vapour. J. Pharm. Innov. 3, 123-133.
3. Watling, D., Ryle, C., Parks, M., and Christopher, M. (2002). Theoretical analysis of the condensation of hydrogen peroxide gas and water vapour as used in surface decontamination. PDA J. Pharm. Sci. Technol. 56:6, 291-299.
4. Watling, D., and Parks, M. (2004). The relationship between saturated hydrogen peroxide, water vapour and temperature. Pharm. Tech. Europe. March, 50-54.
5. Marco-Martin, M-A., Bardat, A., Schmitthaeusler, R., and Beysens, D. (1996) Sterilization by vapour condensation. Pharm. Tech. Europe. 8:24-33.
6. Shimose, L.A., Masuda, E., Sfeir, M., Caban, A.B., Bueno, M.X., dePascale, D., Spychala, C.N., Cleary, T., Namias, N., Kett, D.H., Doi, Y., and Munoz-Price, L.S. (2016) Carbapenem-resistant Acinetobacter baumannii: Concomitant contamination of air and environmental surfaces. Infect. Control Hosp. Epidemiol. 37:7, 777-781.
7. Taneja, N., Biswal, M., Kumar, A., Edwin, A., Sunita, T., Emmanuel, R., Gupta, A.K., and Sharma, M. 2011. Hydrogen peroxide vapour for decontaminating air-conditioning ducts and rooms of an emergency complex in Northern India: time to move on. J. Hosp. Infect. 78:3, 200-203.

Shada Warreth, Senior Bioprocessing Trainer at the National Institute for Bioprocessing Research and Training (NIBRT) is a subject matter expert in Aseptic Processing and Fill Finish Operations. Shada has three years industry experience in QC, QA and production/packaging. Shada joined NIBRT in November 2010 as a Commissioning Technician and is now a Senior Bioprocessing Trainer and a consultant lecturer for distant (online) learning at IT Sligo. She is a member of the PDA. To contact Shada please e-mail: shada.warreth@nibrt.ie

Michael Wood is a biodecontamination specialist providing disinfection solutions to the life science and healthcare markets. He has worked for Bioquell Ireland for the past 5 years and is a member of the educational committee of the Irish Cleanroom Society. To contact Michael, please email: Michael.Wood@Bioquell.com

John Chewins, Director of Scientific & Regulatory Affairs at Bioquell, is an expert in the application of peroxygen-based chemistries to eliminate microbiological contamination. He has worked for Bioquell for over 16 years, developing automated disinfection systems. He is the Deputy Chairman of CEN Technical Committee 216 (Chemical Disinfectants & Antiseptics), an active member of ISO TC 198 (Sterilization & Associated Equipment & Processes) and is a UK expert on the European Airborne Disinfection Taskforce. He has authored a number of publications within the scientific literature relating to biodecontamination. To contact John, please email: John.Chewins@Bioquell.com

VHP (Vapour Hydrogen Peroxide) fragility

Andrew Hopkins

I have been the chairperson for the revision of Annex 1 of the EU and PIC/S GMPS for the manufacture of sterile medicinal products for a couple of years now. As such I engaged with stakeholders and other regulators to understand their wishes and concerns. One particular topic that has come up as a discussion point at a number of the more recent conferences that gives me great concern, and this is around how to sterilise direct and indirect product contact items in an isolator. I therefore felt it was time to go into print regarding the agency's view.

A number of manufacturers are looking at isolator technology in new or existing facilities, which is great to hear, but the fly in the ointment, is that the consideration of how to sterilise direct and indirect contact parts does not always form part of the design process. But before I go further I will clarify what I mean by indirect and direct product contact parts:

- Indirect product contact parts, as the name implies, are equipment parts that come into contact with items and components, such as stoppers. So, although the equipment itself does not contact the product the items that are "processed" by the equipment do.
- Direct contact parts are those that the product passes through, such as filling needles or pumps.

The issue that is arising is that a number of manufacturers are not including robust systems of sterilisation, such as autoclaves, dry heat or offsite irradiation in their facility designs. This leaves a situation where the Agency is being asked why Vapour Hydrogen Peroxide (VHP) cannot be used for "sterilisation" of these direct and indirect product contact parts. After all, pharmacopeias refer to VHP as a sterilising agent. However, our concern is that although under ideal conditions, VHP can achieve a reduction of biological indicator spores of up to 6 logs, the process itself is incredibly fragile.

If we cast our minds back a number of years, when VHP was being used to decontaminate the internal surfaces of isolators (not the indirect or direct contact parts) there were a number of issues seen with biological indicators failing the process due to clumping of spores at a microscopic level. This led to a number of papers being written (such as "Biological indicators don't lie, but in sporicidal gassing disinfection cycles do they sometimes confuse the truth?", European Journal of Parenteral & Pharmaceutical Sciences 2009; 14(1): 5-10 © 2009 Pharmaceutical and Healthcare Sciences Society) that justified biological indicator failure at one or two locations based on statistical analysis. The papers also recommended that a number of indicators (usually 3) be placed at each location to demonstrate a 3 log reduction (which is not a sterilisation process). This, along with other evidence, such as VHP failure due to very minor occlusion, even to the degree that fatty acids from a fingerprint may "protect" contaminating organisms from the VHP demonstrate the true fragility of the process as a sterilant.

If we then consider the design of some of the indirect and direct product contact parts, we find that a number of them are either difficult to achieve VHP penetration, or, damage and wear and tear can leave surfaces that lead to difficulty to clean and therefore potential occlusion.

VHP, when well controlled and validated, is a useful method for the decontamination of the surrounding workspace, e.g. an isolator environment. However, given the above concerns, our current stance is that VHP cannot be used to sterilise critical items. Even if some of the concerns can be removed by well thought out processes, this still leaves the sterilisation at risk of the vagaries of manual process during set up. For instance, how many of us see 'human error' as a high percentage of root cause errors during deviation investigations? Therefore, it would be a high risk option and potentially leave the patient at risk from such a fragile process.

"The issue that is arising is that a number of manufacturers are not including robust systems of sterilisation, such as autoclaves, dry heat or offsite irradiation in their facility designs."

So, what are we expecting?

Our expectation is that the contact parts (direct and indirect) are sterilised using a robust sterilisation method that meets the current requirements of annex 1. This means that:

- The sterilising agent reaches all of the critical surfaces in a consistent and repeatable manner, typically requiring processes such as moist or dry heat sterilisation.
- The item is unloaded from the sterilisation process either wrapped in integral covering or container, or is transferred under grade A conditions, such as a transfer isolator into the manufacturing isolator.

We also expect that the parts are not exposed to the isolator environment until the isolator has been closed and after completion of the work zone decontamination VHP cycle.

We continue to move increasingly into a pharmaceutical world governed by the principles of quality risk management. We are unable to say that VHP will never be an acceptable approach. However, manufacturers who are considering a different approach to sterilisation, or to any other GMP requirement, seek a dialogue with the agency at an early stage. This may save on costly modification later on in the project and who knows, you may even receive some useful help! The GMP Inspectorate can be approached in a number of ways, one is through the Innovation Office www.gov.uk/government/groups/mhra-innovation-office, or by E mail to the GMP Inspectorate directly gmpinspectorate@mhra.gov.uk

This blog was first published in April 2018 in Compliance Matters, a blog of the MHRA Inspectorate.

BioClean™

pure • product • protection

Validated Sterile & Clean Nitrile RABS and Isolator Gloves

We manufacture, test, wash and pack
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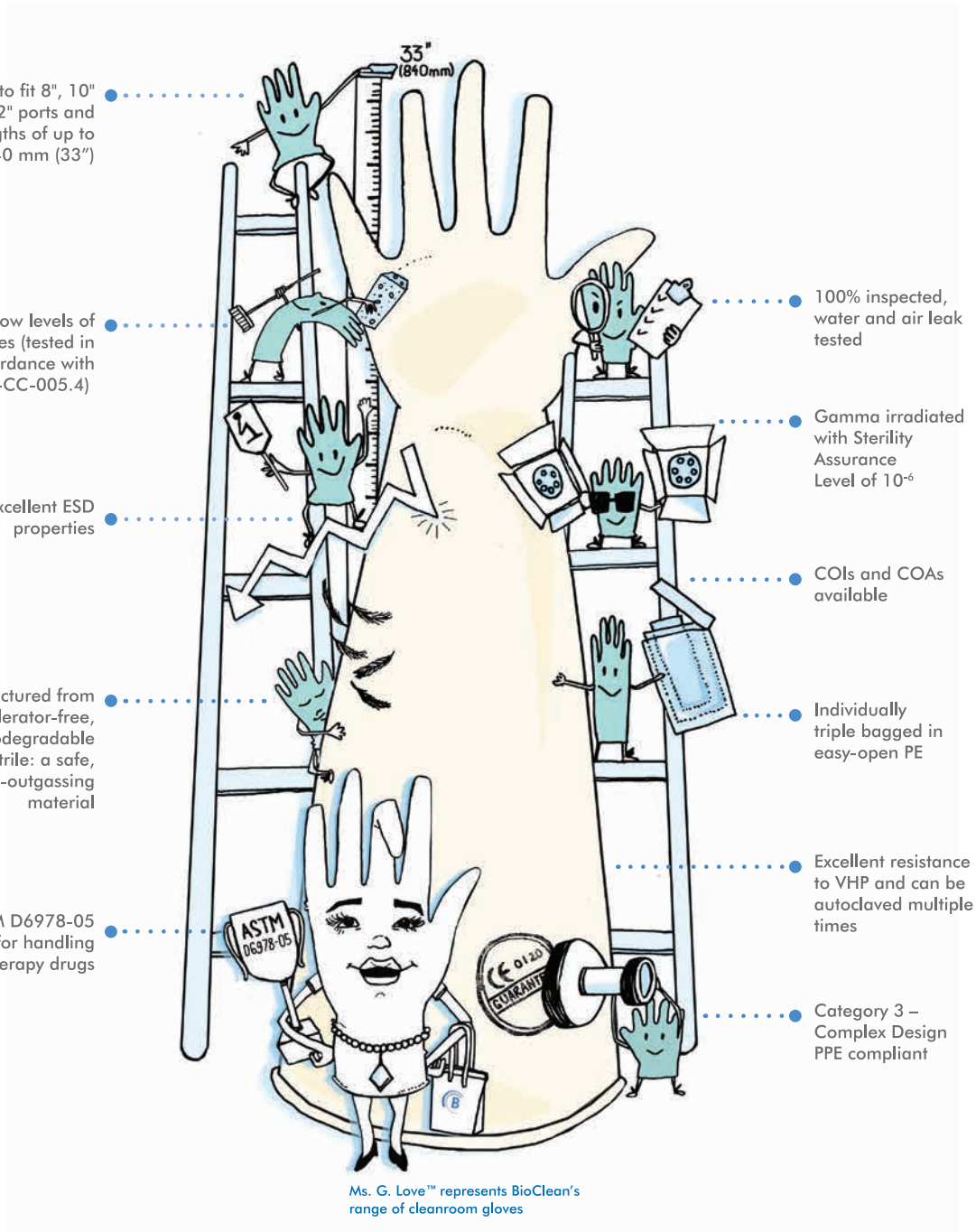


Ms. G. Love™ represents BioClean's range of cleanroom gloves

The BioClean™ sterile EU GMP Grade A compatible nitrile RABS and Isolator gloves range sets the standard for cleanliness and protection. Manufactured and processed using our years of cleanroom knowledge and expertise, our RABS and Isolator gloves will meet the most stringent of cleanroom SOPs. In use around the globe at leading pharmaceutical and biologics manufacturing facilities.

Ansell

For more technical information please visit
www.bioclean.com/RABS-isolator-gloves or email info@bioclean.com

Review of 'Advances in Cleanroom Technology' by Bill Whyte

Gordon Farquharson

The author Bill Whyte is a leading international expert in the field of cleanroom contamination control. He has published over 150 articles and papers through 50 years of research – an amazing compendium of work in the Contamination Control field. The 34 articles chosen for this new book cover immediate post war surgical operating rooms, through to the latest thinking on energy and sustainability in Cleanroom technology. Many of the papers have joint authors and virtually all of them have been subject to peer review.

The book will be of great value across the Cleanroom community from academia, to specifiers and designers, test and certifiers, and of course users.

The book is organised in seven logical technical groups rather than chronological order. This is a really helpful approach allowing the reader to review collections of articles covering historical subjects, application of the principles of risk management to contamination control, and five other subject areas.

The one aspect of the book that really struck me was the way it explores improved understanding and explanation of the science supporting the operations of cleanrooms. Papers in sections 3, 4 and 6 are focused on understanding the strength and nature of contamination sources, and the control mechanisms and performance of non-unidirectional airflow cleanrooms.

The book is bang up to date with the latest papers on particle deposition rate. Bill Whyte sees this as a really exciting development in the characterisation of environmental cleanliness by way of the particles that are likely to deposit on critical surfaces. Some consider that this cleanliness attribute is more valuable than the traditional consideration of airborne sub-micron particles.

Finally, the quality and clarity of printing is exemplary. This is an essential point because most of the papers rely on diagrams, drawings, charts and formulae.

Life-lines

Quotations of Douglas Adams

A common mistake that people make when trying to design something completely fool-proof is to underestimate the ingenuity of complete fools.

Human beings, who are almost unique in having the ability to learn from others, are also remarkable for their apparent disinclination to do so.

The major problem—one of the major problems, for there are several—one of the many major problems with governing people is that of whom you get to do it; or rather of who manages to get people to let them do it to them.

To summarize: it is a well-known fact that those people who must want to rule people are, ipso facto, those least suited to do it.

To summarize the summary: anyone who is capable of getting themselves made President should on no account be allowed to do the job.

Nothing travels faster than the speed of light, with the possible exception of bad news, which obeys its own special laws.

I'd far rather be happy than right any day.

I've come up with a set of rules that describe our reactions to technologies:

1. Anything that is in the world when you're born is normal and ordinary and is just a natural part of the way the world works.
2. Anything that's invented between when you're fifteen and thirty-five is new and exciting and revolutionary and you can probably get a career in it.
3. Anything invented after you're thirty-five is against the natural order of things.

All opinions are not equal. Some are a very great deal more robust, sophisticated and well supported in logic and argument than others.

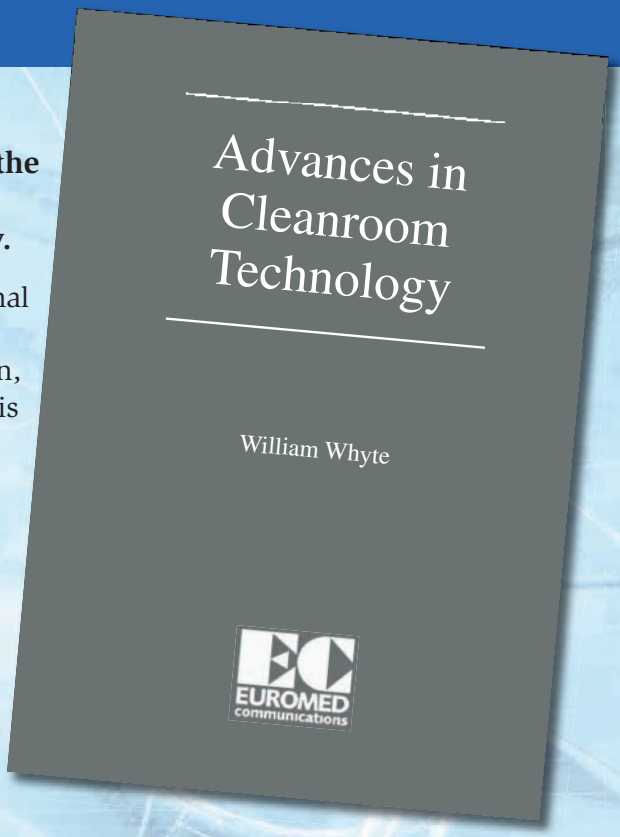
All you really need to know for the moment is that the universe is a lot more complicated than you might think, even if you start from a position of thinking it's pretty damn complicated in the first place.

My doctor says that I have a malformed public-duty gland and a natural deficiency in moral fibre and that I am therefore excused from saving universes.

"What's so unpleasant about being drunk?"

"Ask a glass of water!"

Advances in Cleanroom Technology



This book is based on the author's work that has been published over the last sixteen years to advance knowledge of cleanroom technology.

The author, Bill Whyte, is an international authority on cleanrooms, having been involved for over 50 years in the design, testing and running of cleanrooms. This book is over 500 pages in length and divided into seven sections that group Dr Whyte's scientific writings into topics that include the history of cleanrooms and operating theatres, risk management and risk assessment methods, contamination of products, ventilation design of non-unidirectional airflow cleanrooms, and standard of cleanrooms required for a specified product contamination.

In addition, the book provides further new information on measuring air supply volumes and air velocities, ventilation effectiveness, Computational Fluid Dynamics (CFD), high efficiency air filters, decay of airborne contamination, collection efficiencies of sampling methods, airborne dispersion of particles and MCPs from people, dispersion from floors, transfer of surface contamination, and surface deposition of contamination.

Each of the seven sections is provided with a useful introduction explaining the background to the research and summarising the key points. Overall, this is a book that will prove very useful to anyone involved in any aspects of design, testing and operation of cleanrooms.

For further information and to order see the Euromed Communications website at:
http://www.euromedcommunications.com/

EUROMED communications

Passfield Business Centre, Lynchborough Road, Passfield, Liphook,
Hampshire GU30 7SB, UK
Tel: +44 (0)1428 752222
Fax: +44 (0)1428 752223
email: info@euromedcommunications.com
www.euromedcommunications.com

Cleanroom Technology Conference 2018

Murielle Gonzalez

Feedback

The Cleanroom Technology Conference 2018 has received positive feedback from both delegates and exhibitors.

Held at the National Conference Centre in Birmingham, UK, the two-day event (16-17 May) built on the success of the inaugural edition last year and attracted 600 visitors over the two days, a 58% increase over the footfall registered in 2017.

This year, the accompanying exhibition doubled the number of companies totalling 62 brands on display ranging from cleanroom consumables to monitoring technology and equipment from international manufacturers.

Feedback from exhibitors has been positive. "My congratulations on a great improvement this year in the standard and quality of delegates at the events," said Alan Sweeney, European Clean Process Segment's manager at Camfil.

Commenting on the event, Carl Hunneysett, door division manager, Central Insulations, said: "The Cleanroom Technology Conference is a great opportunity to get up close to new products and understand a wider range of success stories and issues within the industry." Hunneysett commented that not only were these two days a great experience, but also the contacts made and information gathered will really help us going forward. "We will absolutely attend the event next year," he added.

Jean-François Teneul, global life sciences market leader at DuPont, said the event was highly appreciated for different reasons. "First of all, the quality of the organisation and the content of the presentations. All went very well during those two days and the content of the presentations was very adequate to the current context, i.e. GMP Annex 1, barrier systems in cleanrooms, protection of the operators, garments clothing, etc. To me, there was a good balance between presentations and time to spend with the exhibitors. In addition, I liked very much the initiatives of the two workshops (I participated to both of them) and the way it had been done by the speakers. In conclusion, congratulations, and I am eager to come to the next Cleanroom Technology Conference."

The busy exhibition

Delegates have also praised the conference and exhibition for the quality and variety of content in the agenda. "I was very impressed by the event – a lot of very good speakers and a wide variety of exhibitors, plus good networking opportunities and free lunch. Certainly no complaints here!" said Craig Bradford, of the technologist environmental monitoring group at Abbott?

Paul Hurren, pilot plant and validation leader at Reckitt Benckiser Healthcare, concurred: "Just wanted to thank you for an excellent two days, very insightful and a great opportunity to see new developments in all things cleanrooms," he said.

Cleanroom Technology Awards

In addition to a content-packed agenda, the event debuted the Cleanroom Technology Awards.

Four award categories were introduced to recognise and reward achievements in the industry, two of these celebrated the best product innovations from those exhibiting at the Cleanroom Technology Conference 2018.

The Best Cleanroom Facility and the Best Cleanroom Innovation were judged by John Neiger, editor of Clean Air and Containment Review and Susan Birks, former editor of Cleanroom Technology magazine.

Connect 2 Cleanrooms (C2C) received the Best Facility Award. The company was recognised for the cleanroom construction it delivered for medical technology group Convatec. The judges praised the project because it was broad in scope and showed careful consideration of aesthetics, energy efficiency and sustainability while meeting budget and timeline constraints, and making good use of the latest build technology and methods.

The judges felt that the project by Cleanroom Solutions delivered to the University of Cambridge Graphene Centre (Electrical Engineering) deserved a 'Highly Commended' award because of its "impressive technical complexity".

The Best Innovation Award was attained by Honeyman Group for its HydroGienic, a patented pharmaceutical water distribution system. This game-changing innovation provides economic advantages and ease of installation as well as flexibility, sustainability and overall operational benefits.

Kimtech received the Best Exhibitor – Product Award for its A5 Sterile Cleanroom Coverall while Air Techniques International won the Best Exhibitor – Technology Award for the AC100H microbial air sampler by Lighthouse World Wide Solutions.

Tim Triggs (second left) and Mark Wilson (fourth left) of Air Techniques International receiving the Best Exhibitor – Technology Award from Gordon Farquharson with Murielle Gonzalez (left)

Speakers and workshops

Two 30-minute workshops debuted this year. Connect 2 Cleanrooms delivered a session on rotational cleaning. The workshop focused on understanding the process as well as its benefits. The second workshop focused on designing a bespoke gowning procedure. Delivered by Nigel Slater, director CM Supply, the session outlined basic operator preparations for entry into a cleanroom, the pros and cons of different garment systems currently available in the market, and offered advice on identifying the best gowning procedure for a particular application.

The conference discussed 16 topics presented by highly-experienced professionals in the cleanroom and contamination control sectors. While day one focused on regulation and standards, day two focused on all things related to operation.

Gordon Farquharson, MD Critical Systems Limited, chaired day one and presented the current revision to Annex 1 of the EU GMP/ISO 14644. He made it clear that the final document is yet to be released, but that the update adds the concept of risk-based thinking to manufacturing processes. The session was followed by Joe Hughes, GMP validation consultant, on how to prepare for GMP audits.

Other presentations looked at data integrity, the life cycle approach to disinfection, how to deal with extractables and leachables, and microbial consideration in cleanroom validation. An update on the current revision of ISO 14644-3 – the standard that specifies test methods for cleanrooms and clean zones – and a presentation on the design and implementation of a real-time monitoring system completed the day's presentation.

Chaired by Tim Triggs, UK general manager EMEA director, Air Techniques International, day two focused on all things operation. Triggs presented the ISO 14644 Part 4 commenting on design, construction and energy standards. It was followed by a presentation on key consideration for setting up a cleanroom, from concept to operation.

Presentations on manufacturing cleanroom technologies for the industry 4.0 and cleanroom design considerations for highly potent active pharmaceutical ingredients, (HAPIs) led to the sessions on HVAC systems and cleanroom disinfection. Cleanroom garments and the new standard in air filtration, its impact on cleanrooms and HEPA filters closed the agenda. The organising team will shortly start work on the content for the Cleanroom Technology Conference 2019. Dates and venue will be announced shortly.

This report is published by kind permission of Cleanroom Technology. The author, Murielle Gonzalez, is editor of Cleanroom Technology.

Connect 2 Cleanrooms wins Best Cleanroom Facility Award at Cleanroom Technology Conference 2018

Connect 2 Cleanrooms was honoured to receive the Best Cleanroom Facility Award at the recent Cleanroom Technology Conference 2018. This was yet another award for the company and was in recognition of the project it delivered for Convatec, a global medical products and technologies company. Connect 2 Cleanrooms is an industry leader, creating cleanroom solutions for critical environments both in the UK and internationally. Established in 2002, the company designs and manufactures hardwall, softwall and panel system cleanrooms in-house - delivering quality cleanroom solutions to meet the ISO 14644-1: 2015 standard required. The company provides validation for cleanroom facilities and biosafety cabinets and qualifies that they are operating and performing in conformance with the Cleanroom Standards with a tailored testing schedule. Cleanroom training is also available to educate operators on how to minimise contamination risks through the correct implementation of procedures. Its consumables division, cleanroomshop.com, supplies a full range of consumables, equipment and furniture to the cleanroom industry worldwide.

Phone: +44 (0) 1524 812899, E-mail: info@connect2cleanrooms.com or Web: www.connect2cleanrooms.com

Take-off for CRC's designs on space

Clean Room Construction (CRC) is over the moon to have secured more cleanroom design and build projects for ground-breaking space-age facilities.

CRC has been contracted to deliver the next stage of a prestigious project at RAL Space in Oxfordshire to design and build a suite of cleanrooms to test satellite components. CRC has previously engineered a suite of 15 cleanrooms for RAL Space - the space department of the Science Technology Facilities Council (STFC). These facilities are used for the assembly and testing of satellite instrumentation for future space missions and have attracted major international media attention.

CRC has also won a contract to design and build cleanrooms for the testing of deployable antennas at Oxford Space Systems' (OSS) new facility at the Harwell Space Cluster in Oxfordshire. HRH the Duke of York visited the site last month and praised the global centre for pioneering space technology.

CRC Managing Director Steve Lawton said: "These projects really are out of this world. Companies like RAL Space and Oxford Space Systems are addressing some of the greatest global space challenges and it's a great privilege for CRC to play a part in this mission."

For more information on CRC see www.crc-ltd.co.uk

Contec Rotational Disinfectants

Contec have recently launched Contec CyChlor, a hard surface disinfectant based on 600ppm hypochlorous acid. Developed to be used every day with broad spectrum efficacy against bacteria and yeasts, Contec CyChlor can be rotated with Contec ProChlor; 2000ppm hypochlorous acid, when a powerful sporicidal disinfectant is required. Available sterile and filtered, Contec CyChlor is fast acting with a validated contact time of 3 mins for bacteria and yeasts.

Hypochlorous acid is a powerful hard surface disinfectant, 100 times more efficacious then sodium hypochlorite (bleach), allowing a lower concentration to be used, thereby reducing residues and operator and environmental hazard. Contec's hypochlorous acid disinfectants are unique in the way they are manufactured, creating a ready to use product with a 2 year shelf life

For more information about Contec CyChlor or to request a sample email infoeu@contecinc.com

Top marks for Cherwell's Redipor® prepared microbial media products

A recent customer satisfaction survey has affirmed that the vast majority would recommend Cherwell Laboratories and its Redipor® microbiological media products to a colleague. Value for money, excellent customer service and product quality were all key factors contributing to the very positive outcome of this survey. These results are evidenced by Redipor's growing user base within the pharmaceutical and associated industries, both domestically and across Europe. Therefore, to accommodate all customers, Cherwell now has both UK and Euro versions of its 2018/19 Redipor Prepared Media price list available to download from Cherwell's website.

Redipor prepared media products scored highly with customers in Cherwell's recent survey to achieve an impressive Net Promoter Score of +76 (from a range of -100 to +100). Customer comments as to 'Why Cherwell?' included: "The excellent service; great pricing; exceeding expectations with delivery times; helping us out in a crisis; flexibility by preparing bespoke media; pragmatic advice; and realistic timeframes. What more could anyone want?"

The Redipor® prepared microbiological media range is available in a wide variety of formats.

For more information, see www.cherwell-labs.co.uk

‘Cleanzone Campus’ – expanding cleanroom knowledge through research

Universities and research institutes are drivers of innovation for industry – particularly in the highly dynamic field of cleanroom technology. With Cleanzone Campus Messe Frankfurt has created a platform where research institutes in this field can present their projects. Of the institutions already signed on, Albstadt-Sigmaringen University will present their current projects in cleaning and hygiene technology. One concerns round robin testing as a means of standardising procedures for the preparation of cleaning textiles (e.g. wiping cloths and covers etc.). Another addresses the potential offered by technical cleanroom systems for food processing. OTH Amberg-Weiden will also present projects in cleanliness and hygiene and has an ISO class 7 cleanroom where students in the medical technology faculty can familiarise themselves with theoretical and practical cleanroom technology. The Fraunhofer Institute for Manufacturing Engineering and Automation (IPA) will show a mobile and flexible cleanroom tent and the ‘FlexNote’ IT communication tool. Finally, the primary focus at the Hermann-Rietschel-Institut is cleanroom hygiene including keeping concentrations of chemically, physically or biologically active aerosols as low as necessary and experimental and numeric studies on the dispersal and sedimentation behaviour of articles in enclosed spaces. HRI will present the findings from their most recent projects concerning cleanrooms, operating theatres and special isolation wards.

Cleanzone is from 23 – 24 October in Frankfurt, Germany – see https://cleanzone.messefrankfurt.com/frankfurt/en.html

China is home to twelve thousand cleanroom enterprises – by Cleanroom Guangzhou Exhibition Committee

With the adoption of cleanroom technology ramping up in various industries in China, there has been a proliferation of cleanroom enterprises in the last decade. By looking at 2018 China company registration data, Guangdong Association of Cleanroom Technology (GACT) have counted the total of Chinese cleanroom enterprises (Hong Kong, Macao, Taiwan excluded) to be over twelve thousand, more than 60% of which are from Guangdong and Jiangsu Province.

Here is the detailed data of Chinese cleanroom companies released by GACT:

	China total	Guangdong Province		Jiangsu Province	
Category	Number of Companies	Number of Companies	% share of national	Number of Companies	% share of national
Cleanroom Technology	947	144	15	176	19
Cleanroom Engineering	1,097	247	23	247	23
Cleanroom Equipment	1,321	240	18	293	22
Cleanroom	9,118	2,451	27	4,139	45
Total	12,483	3,082	25	4,855	38

The strong demand in China has not only spawned the emergence of home-grown cleanroom enterprises, but also opened up extensive opportunities for overseas companies.

If you are interested in sourcing quality Chinese suppliers, please sign up as visitor for Cleanroom Guangzhou Exhibition 2018 via http://clcte.com/order/order.php?id=46.

For those who aspire a share in Chinese market, please contact Cleanroom Guangzhou Exhibition Committee via Mae Law (maelaw@163.com), and become our exhibitor today!

Crowthorne Group extends research into the best methods to destroy contaminants for CL3 & CL4 facilities

As the debate between different fumigation methods continues, Crowthorne Group has been researching the efficacy of Chlorine Dioxide to kill spores in CL3 and CL4 laboratories, compared to the VHP and Formalin methods. Initial studies suggest that Chlorine Dioxide is most effective at high spore concentrations, and spores appear more sensitive to the cumulative dose of ClO_2 than just exposure time and concentration. Previous tests in hospital settings were inconclusive in reducing bacterial load further than other methods.

All these methods are offered by Crowthorne, and the selection of the correct route to maximize the kill is paramount; depending upon contamination loads, working methods and layout of the lab, ability to control humidity and temperature, and the presence of proteins and prions.

The next phase of research is to establish which contaminants are destroyed most effectively by each method so as to advise customers on the likelihood of a good result after the process is complete; if you are paying for a fumigation you want to get the best possible kill for your money and downtime.

Contact: +44 (0)1252 372333/ sales@chts.co.uk (UK) or +353 (0)1824 3670/ info@bpscrowthorne.ie (Ireland)

Events

Dates	Event	Organiser
2018		
August 16-18	Cleanroom Guangzhou 2018, Guangzhou (Canton), China	Guangzhou Grandeur International Exhibition Group
September 11	PHSS & UCL Q3P Annual Conference 2018	London UK
September 23-26	ISCC 2018, Hague, the Netherlands	VCCN
October 23-24	Cleanzone 2018	Messe Frankfurt
November 12-15	IEST Fall Conference, Schaumberg, Illinois	IEST
2019		
April 29 – May 2	ESTECH 2019, Las Vegas,Nevada	IEST
November 12-15	Fall Confenence, Rosemont, Illinois	IEST

Training courses

IEST (Institute of Environmental Sciences and Technology) www.iest.org		
2018	**Event**	**Location**
November 12	Cleanroom Basics: What Is a Cleanroom and How Does It Work?	IEST Fall Conference Schaumburg, Illinois
November 13	Beyond Cleanroom Basics: Fundamental Information for Cleanroom Operations	IEST Fall Conference Schaumburg, Illinois
November 14	Cleanroom Classification Testing and Monitoring	IEST Fall Conference Schaumburg, Illinois
November 15	Understanding the Cornerstone Cleanroom Standards: ISO 14644-1 and 14644-2	IEST Fall Conference Schaumburg, Illinois

ICS (Irish Cleanroom Society) www.cleanrooms-ireland.ie		
2018	**Event**	**Location**
September 14	GMP Cleanroom Cleaning (Basic)	Dublin, Ireland

S2C2 (Scottish Society for Contamination Control) www.s2c2.co.uk		
2018	**Event**	**Location**
November 6-8	Cleanroom Testing and Certification (CTCB-I)	Coatbridge, Scotland
November 21	Cleanroom Technology (CTCB-I)	Letchworth, England, Scotland

R3Nordic www.r3nordic.org		
2018	**Event**	**Location**
October 2-4	Cleanroom Testing and Certification (CTCB-I)	Göteborg, Sweden

VCCN (Association of Contamination Control Netherlands) www.vccn.nl/english
For a complete list of courses including CTCB-I courses, please see www.vccn.nl/agenda

Note:
CTCB-I Certification: Cleanroom Testing and Certification Board International Certification, see CTCB-1 website: www.ctcb-i.net/index.php

ISCC'18

INTERNATIONAL SYMPOSIUM ON CONTAMINATION CONTROL

THE NETHERLANDS THE HAGUE 23-26 SEPTEMBER '18

THE WORLD BEHIND CONTAMINATION CONTROL

From 23 to 26 September 2018, the Biannual International Symposium on Contamination Control (ISCC) will be held. The symposium will take place at the World Forum in The Hague.

Contamination control is essential to all high-tech industries and research facilities where 'cleanliness' is a precondition for the quality of the product and for the safety and health of the users or employees.

New research results and innovative technological applications make it possible to keep improving our control over air purity. The world's leading researchers and experts will share their vision and knowledge on their innovations and cases. So meet us at ISCC'18, and learn everything about "the world behind Contamination Control."

Health, Life Sciences, Micro-Nano, Photonica, Micro Assembly, Food

REGISTER NOW!

REGISTER AT **ISCC2018.COM**

ISCC'18
INTERNATIONAL SYMPOSIUM ON CONTAMINATION CONTROL
THE NETHERLANDS | THE HAGUE

TIME	PROGRAMME MONDAY 24 SEPTEMBER
08:00	**REGISTRATION**
08:30	**OFFICIAL OPENING ISCC'18**
09:15	**KEYNOTE SPEAKER 1** **Dave Blank, University Twente**
10:00	**BREAK** AT THE EXHIBITION
10:30	**Outdoor airborne contamination in hospitals and cleanrooms** • Cleanroom airborne contamination in relation to outdoor airborne contamination *Michel Thibaudon* • Development of the guideline for the classification and testing of air permeability of the cleanroom envelope and similar controlled environments *Harm van den Oever* • Ultra fine dust and health with controllable deposition of Nano structured particles in clean rooms and other technologies *Bob Ursum*
10:30	**How technical trends enhance selection and performance monitoring of garments** • New selection criteria of protective garments for cleanrooms and controlled environments *Steve Marnach* • To reuse or not to reuse: a global study on the performance of cleanroom garments over their life cycle *Matheus Rodrigues Barbosa* • The digitalization of cleanrooms *Dennis Smeijer and Arthur Lettinga*
10:30	**Requirements for space and photonics +...** • Biocontamination control in space industries: a general overview *Markus Keller and Udo Gommel* • Contamination study of space sensitive surfaces by packaging materials *Delphine Faye* • From clean machine to… *Philip van Beek*
10:30	**Contamination in Laser Optics** • Research on precision cleaning technologies for large aperture optics *Xiao Dong Yuan* • The study of laser induced damage owing to surface contamination for lager aperture optics in high power laser facility *Xin Xiang Miao* • Study of organic contamination removed by plasma cleaning technology for critical surface *Hao Liu*
11:45	**Risk analyses in life science** • Cleanrooms or containment suites – common features and differences - The devil is in the detail *Per Staugaard* Why establishing control proves to be difficult *André van Tongeren* • Proposed Changes to EU GMP Annex 1 & Draft Revision ISO-DIS 14644-3:2016 *Sheesh Gulati*
11:45	**Design and construction** • Cleanroom zoning, the challenge of pressure differential and flow *Frans Saurwalt* • Clean and protective environment – CAPE *Udo Gommel* • Ventilation Equations *Andrew Watson*
11:45	**Food industry** • Contamination control and hygienic design in the food industry *Frans Saurwalt*
11:45	**OR design from a different perspective** • Hospital project in Brasil *Antonio Gamino* • Contamination control in displacement ventilated operating theaters *Fransesco Romana* • Ozon cleaning in OR's *Johannes K-M Knobloch*
13:00	**LUNCH BREAK** AT THE EXHIBITION

TUTORIAL 1: Cleanroom requirements *Koos Agricola and Connor Murray*
• Risk assessment (Product, Process, FMEA, HACCP)
• Cleanliness (air, surface and transfer (deposition) and standards
• Contamination control solutions
• Requirements (application)
+ WORKSHOPS

TUTORIAL 1 + WORKSHOPS

TIME	PROGRAMME MONDAY 24 SEPTEMBER
14:00	**Practical approaches towards developing life science facilities** • Case study on hospital aseptic compounding facilities and radiopharmacies *Conor Murray* • Guidelines central sterilization department *Paul Joosten* • Digitizing the interpretation process in environmental monitoring *Jean-Paul Sanders*
14:00	**Energy management** • Analysis of operation and energy consumption of hospital's isolation room *Wim Zeiler* • Ventilation eff improvement *Paul Molenaar* • Modern PTFE membrane based HEPA/ULPA filters for improved energy savings and risk reduction *Marc Schmidt*
14:00	**Monitoring air and surface cleanliness (technical applications)** • Environmental Monitoring *Jason Kelly* • Traceable calibrations *Edwin den Hartog* • Fast particle cleanliness monitoring of high tech product surfaces *Anton de Jong*
14:00	**ICCCS STANDARDS** • ISO TC209 new cleanroom standards and outreach projects I *Berthold Duthorn* • ISO TC209 New cleanroom standards and outreach projects II *Daqain Wang*
15:15	**BREAK** AT THE EXHIBITION
15:45	**Operating theatre contamination** • A comparison between measured values of airborne viable particles and calculated values with the dilution principle in operating rooms with low velocities unidirectional air flow systems *Bengt Ljungqvist* • Distribution of microbial contaminants in operating theatres and healthcare environments *Eugen Lichtmer* • Contamination control in operating theatres *Remko Noor*
15:45	**Safety and standardisation challenges for life science facilities** • Preparing parenteral nutrition formulations: hospital pharmacy compounding department *Matieu Wasiak* • Development and status of the CEN Biocontamination control project (European standard) *Michel Thibaudon* • Requirements for detergents used in non sterile pharmaceutical applications *Thomas Altmann*
15:45	**Contamination risk in semi conductor industry** • New method for the assessment of condensed contamination by chemicals onto surfaces (SCC) *Vanessa Pfenning* • Think outside the box: film type contamination, their impact and ways of detecting and avoiding *Marcel Kleßen* • Residual gas analysis as tool for material screening for UHV applications and comparison to other emission test methods *Markus Keller, Udo Gommel*
15:45	**In use monitoring of operating theatres** • Introduction of VCCN guideline 8: In use monitoring of operating theatres *Robero Travesari*
17:00	**KEYNOTE SPEAKER 2** **Bas Zaat, Amsterdam Medical Center**
17:45	**DRINKS** AT THE EXHIBITION
19:00	**BANQUET** AT LOUWMAN MUSEUM

TUTORIAL 2: Establish Control *Frans Saurwalt and Arnold Brunner*
• Program of Requirements (applications)
• Cleanroom concepts
• Design and Construction
• Operational procedures
+ WORKSHOPS

TUTORIAL 2: Establish Control *Frans Saurwalt and Arnold Brunner*
• Program of Requirements (applications)
• Cleanroom concepts
• Design and Construction
• Operational procedures
+ WORKSHOPS

TIME	PROGRAMME TUESDAY 26 SEPTEMBER
08:00	**REGISTRATION**
08:30	**KEYNOTE SPEAKER 3** **Vadim Banine, ASML**
09:15	**Contamination monitoring** • Development and use of thermally generated aerosol for clean room airflow visualisation testing and HEPA filter challenging *Trevor Dunnington* • ISO 14644-3 B7 installed filter leakage tests - a comparison and guidance *Tim Triggs* • Magnetic Field Interference – A Rising Consideration for Semiconductor Fab and Process Tool Design *Wolfgang Eissler*
09:15	**Establishing contamination control for future proof hospitals** • Industry innovation agenda on contamination control in hospitals *Roberto Traversari* • Standard developments for operating theatres and isolation rooms in Europe *Frans Saurwalt*
09:15	**Contamination risks and control solutions for electromechanical devices** • Contamination control applied to inkjet printhead *Koos Agricola* • Creating, implementing and maintaining a monitoring plan based on Risk Assesment *HaŞim Solmaz* • Risks due to the use of cleanroom technology components *Joachim Ludwig*
09:15	**Biosafety risks and preventions** • Analysis of cross-infection in a hospital's isolation room *Ilse Schoenmaker* • High containment BSL 3-4 *Paul Joosten* • Biosafety cabinet with air isolation system (AIS) for tissue engineering *Naoki Ogawa*
10:30	**BREAK** AT THE EXHIBITION
11:00	**Design and construction** • Offsite construction – the latest innovation in global cleanroom manufacturing *Rowin Vos* • Clean build protocol *Andrew Watson* • POD's offsite vs site constructed flexible modularcleanroom approaches *Conor Murray*
11:00	**General standards** • ISO/DIS 14644-15: Assessment of suitability for use of equipment and material by airborne contamination by chemicals (ACC) *Markus Keller* • Comparison of the photometer and airborne particle counter methods for integrity testing of HEPA and ULPA filters according to ISO 14644-3 *Bernard Thaveau* • Cleanliness behaviour of Consumables; PWI *Udo Gommel*
11:00	**Contamination control in semiconductor industry** • Vacuum spikes: effects and control of contamination on vacuum sealing surfaces *Konstantinos Gkrekos* • Design, setup and testing of an noninvasive airborne moleculair contamination monitoring system for a front-opening unified-pod for sub 10nm semiconductor manufacturing process *Bryan J. Puruncajas M.* • Cleanliness quantification of wafer metrology systems *John Timmermans*
11:00	**Cleaning and disinfection** • Cleaning and disinfection programs part of a lifecycle approach: future Annex 1 requirements *Walid El Azab* • Development of a harmonised method for cleanroom hard surface disinfectant efficacy evaluations *Rachel Blount* • Management of non-viable particle excursions in the context of the new ISO14644-2 *Olivier Chancel*

TUTORIAL 3: Cleanroom operations *Philip van Beek and Chris Delaney*
• Cleanroom behaviour
• Cleaning
• Maintenance
• Procedures (applications)
+ WORKSHOPS

TUTORIAL 3 + WORKSHOPS ▶

TIME	PROGRAMME TUESDAY 26 SEPTEMBER
12:15	**LUNCH BREAK** AT THE EXHIBITION
13:15	**Operations in space industry** • Evaluation of decontamination process adapted to large optical components *David Cheung* • Statistical illustration of cleaning method efficiencies for flight hardware surfaces *Thomas Jordan* • Particulate contamination size distribution on optical systems evaluation *Sabine Dagras*
13:15	**Particle deposition and surface cleanliness** • CLEAPART-100 to monitor particle deposition rate in laser cleanrooms *Isabelle Tovena Pecault* • The PFO 1000 Monitor: A novel real-time, in-situ, automated instrument for monitoring particulate fall-out in clean environments *Andrew Holland* • Particle deposition rate applications *Koos Agricola*
13:15	**Effective control pharmaceutical manufacturing** • Case studies of recurrent microbial contamination - benefit of EM data review and periodic audit of practices *Walid El Azab* • Microbiology single use impactor head *Frank Panofen* • Cleanliness assessment and cleaning validation of medical devices *Udo Gommel*
14:30	**BREAK** AT THE EXHIBITION
15:00	**KEYNOTE SPEAKER 4** **Peter Ros, Futurologist**
15:45	**CLOSING CEREMONY**

TUTORIAL 4: Demonstrate control *André van Tongeren and Robert Mielke*
• Measurement methods
• Verification
• Monitoring
• Applications
+ WORKSHOPS

PROGRAMME ISCC'18 WORLDFORUM THE HAGUE

ISCC'18
INTERNATIONAL SYMPOSIUM ON CONTAMINATION CONTROL
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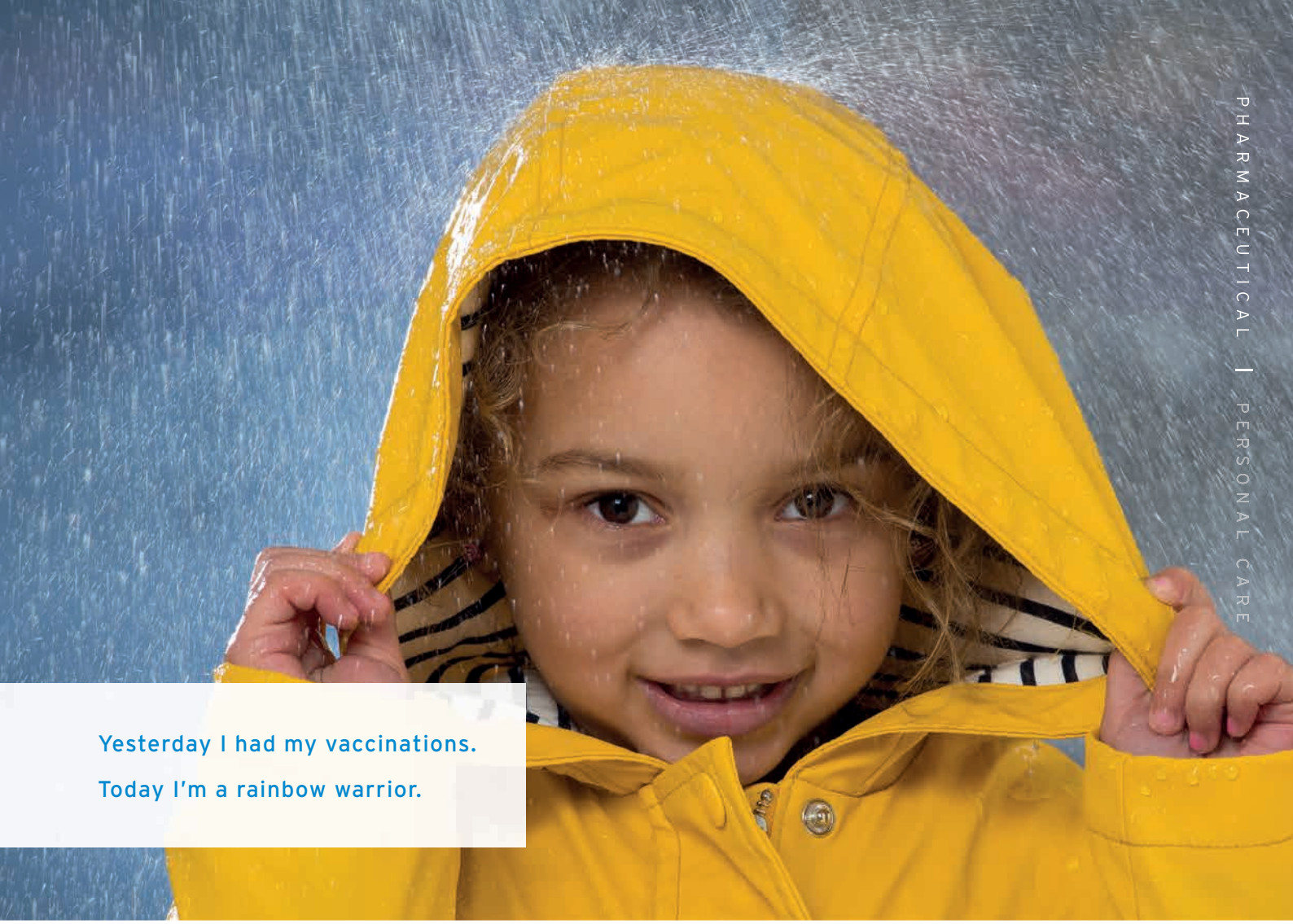

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