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Picture: Envair + ONFAB are specialist containment engineers

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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Contents

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Editorial

Those of you who know me know that I have had a series of total knee replacements (TKRs), five in all, in my right knee. A recent conversation with Bill Whyte has prompted me to write about how it all started.

I was in my room in a private hospital recovering from my first TKR operation when I heard a commotion in the corridor outside. It sounded as though someone had fallen, but I also heard a big splosh of liquid. This was followed by the footsteps of people hurrying to attend and anxious voices. When the commotion had died down, I asked one of the staff what had happened. She told me that the patient in the room across the corridor had developed a very serious infection following a hip replacement. They had been walking him down the corridor – mobilising him – when the infection had burst and he had fallen. He was under the same surgeon as me.

A little while later, the surgeon was on his ward rounds. He had just spent some time with his infected patient and he came into my room holding out his hand to shake mine. (After a few more visits from him, I observed that shaking hands was the main part of his interaction with his patients). It was only several weeks later, when my own infection became apparent, that I reflected on his attention to hygiene and infection control. Had he disinfected his hands after seeing his severely infected patient and before shaking mine? More importantly, what had gone on in theatre during my own operation? How was it that two of his patients had become infected? My infection could have been from any one of a number of causes. All I knew was that it was *Enterobacter cloacae* and that having spent a large part of my career in the clean air business, including ventures into ultra clean air theatres (UCAs), I had ironically become the wrong sort of statistic. Readers will understand my strongly held view that every measure possible should be taken to reduce the possibility of post-operative infections in all types of surgery, especially in orthopaedic surgery where bone infections are so difficult to cure. My third TKR also resulted in a bone infection.

In my conversation with Bill Whyte, he asked if I was aware that in 2016, the World Health Organization had published global guidelines for preventing surgical site infection (SSI)[1] that included a recommendation that "laminar airflow ventilation systems should not be used to reduce the risk of SSI for patients undergoing total arthroplasty surgery." This was qualified as a conditional recommendation on account of "low to very low quality of evidence." Bill drew my attention to his own paper, co-authored with B. Lytsy, published in the *Journal of Hospital Infection* in 2019.[2] The paper notes that the WHO recommendation contradicts and indeed ignores information published in earlier major studies carried out by Charnley as well as those carried out by the UK Medical Research Council (MRC). The paper also suggests reasons why some recent studies have failed to demonstrate that ultra clean air (UCA) systems reduce deep joint infection after total joint arthroplasty (TJA). The MRC study, referenced in Bill's paper, was based on information from 19 hospitals in the UK and Sweden and 8136 operations. It showed that there was clear relationship between airborne concentrations of MCPs (microbe carrying particles) and deep joint infections. Bill's opinion was that UCA systems are essential for total joint replacement operations. It seems common sense that unidirectional airflow (UDAF) systems which, typically, reduce the MCP concentration by about 100 times should be installed in operating theatres

In a hard-hitting editorial "Massacre of the Innocents[3]" in the *European Journal of Parenteral & Pharmaceutical Sciences* where he was Editor in Chief for a number of years, the late John Sharp wrote "reports have indicated that [in the UK] every year 5000 people die from infections contracted in hospitals – more than are killed on the roads" and went on "Compared to the appalling hazards of the Health Service, the risks from faults in manufactured medicines pale into complete insignificance. The most dangerous place to be in Britain today is in hospital. Why, then, devote so much regulatory effort to inspecting pharmaceutical manufacturers? Why not use those same resources to inspect hospitals, and to enforce appropriate standards of patient care?" JN

For references see page 19.

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Standards for pharmaceutical isolators: an overview

Tim Coles

Abstract

Pharmaceutical isolators have wide application in critical processes such as aseptic filling and genetic engineering, and yet they are not covered by any specific UK, or international standard. At present, users have to rely on standards essentially written around cleanrooms, which are a very different contamination control system. There is also one standard which is a sub-section of an aseptic processing standard. This paper highlights areas where these existing standards are perhaps deficient.

Existing isolator standards and guidelines

When gloveboxes first came into general use in the pharmaceutical industry, around 40 years ago, there were no specific standards available to give guidance on their design, construction and operation. Today, decades on, there is still no standard directly relating to what we now term 'isolators'. Instead, we rely on a mixture of cleanroom standards such as the ISO 14644 series of standards[1, 2, 3, 4, 5, 6] and containment standards such ISO 10648.[7, 8] Perhaps the most focussed current document is ISO 13408-6; 2005.[9] At the time of writing this standard is under periodic review at the DIS (Draft International Standard) stage – ISO DIS 13408-6.[10] It is also just one part of a standard devoted to aseptic processing, thus leaving aside the all-important containment aspect of isolator technology. There are also guidelines such as the book *Pharmaceutical Isolators*[11] and, of course, *EU GMP Annex 1*.[12]

Where aseptic applications are concerned, ISO 14644 is useful and informative, but it has a fundamental flaw in relation to isolators: cleanrooms are manned by human operators. As a result, the greater part of these standards are devoted to the means to first minimise, and then to manage, the particulates generated by personnel. Isolators, by definition, do not have to accommodate human operators and, as a consequence, are liberated to be designed, constructed and operated in completely different ways.

One very significant advantage of isolators over cleanrooms, in aseptic operation, is the capacity for gas-phase or aerosol bio-decontamination. Hydrogen peroxide has become the biocidal agent of choice for sound reasons but, here again, there are no definitive standards. However, ISO DIS 13408-6 does provide considerable discussion, and the PHSS Guidance Note No. 1[13] gives a lot of practical guidance following MHRA comment on the application of vapour phase hydrogen peroxide in isolator bio-decontamination.

Where toxic or pathogenic applications are considered, ISO 10648 is again useful and informative, but essentially comes out of radiological protection, and is very dated. Significant advances have been made in containment isolators over the last 25 years and therefore design, construction, testing and operation standards are surely due for review.

Where the application is both aseptic and toxic, as for example in the preparation of cytotoxic parenteral solutions, the ISO standards 14644 and 10648 are of limited use since neither cover this situation, and ISO DIS 13408-6 is technically not applicable.

It is clear that both aseptic and containment isolators offer major advances over previous technology, but neither is covered by specific standards. The UK Pharmaceutical Isolator Group (UKPIG) did start down this route, but the organisation effectively closed down in 2005 when the driving force, Brian Midcalf,[i] retired. Standards in general, and ISO standards in particular, take a long time to develop and be published, often years and sometimes decades, as in the case of EU GMP Annex 1. It seems unlikely that any individual or group is likely to take up the official challenge in the near future, but perhaps some unofficial draft standards could be drafted in the meantime.

What aspects of isolator technology might such drafts tackle, where the current standards fall short? One is the apparent anomaly in airborne particulate figures, where EU GMP Grades A and B do not seem appropriate for isolators. Although the industry should be adopting ISO standards for airborne particulates, many operators still prefer to use the EU GMP designations. Both Grade A and Grade B permit up to 3,520 particles of ≥0.5µm per m^3. In terms of isolator technology, such a particle burden is appalling! Even a turbulent flow isolator will give virtually zero particle count at rest. If an isolator gives ≥0.5 µm particle counts above a few tens, there is likely to be an investigation. Why then do we apply cleanroom standards to isolators? The regulators in general, and the MHRA in particular, are keen to advance the technology of pharmaceutical production where possible. This being the case, the particulate standards for isolators need to be addressed to match the achievable results.

The threshold limits for airborne particles in isolators might perhaps look something like the values shown in Table 1. These are all very much lower than the

Table 1: Suggested maximum number of particles ≥0.5 µm per m^3 for isolators

	Unidirectional flow isolator	Turbulent flow isolator
At rest	5	50
In normal operation	50	500

i. Brian Midcalf very sadly died in 2019.

3,520 particles allowed under both A and B grades of EU GMP Annex 1.

Some guidance would be needed as to how and where particle counting is to take place in the isolator.

Total particle counts of course include the all-important sub-set which are the viable particles. Here again, the much better environmental conditions inside isolators offer the possibility of setting more stringent standards, however it may not be possible to set better values than those tabulated in the EU GMP for purely practical reasons. *Pharmaceutical Isolators* offers a set of viable particle limits for isolators and states "This represents a reduced acceptance level for settle plates compared to the EC[sic] GMP guidance." This probably represents the current best standard for viable particles in isolators.

Moving on, it would seem reasonable to set some standards for the basic functional aspects of isolators. It is primarily the flow of HEPA filtered air through isolators which provides the clean conditions. In unidirectional airflow (UDAF) isolators, which are normally downflow, the requirement is easily defined as the conventional 0.45 m/s, plus or minus 20%. However, an isolator standard might present a requirement to demonstrate unidirectional airflow down to a specific height above the work surface. A suggested minimum make-up air flow rate might also be proposed, for example 10% of the unidirectional airflow. In the case of turbulent flow isolators, an isolator standard should set a minimum air change rate of perhaps 60 total air changes per hour. It could go on to require demonstration that the turbulent flow purges all parts of the isolator volume, and that there are no standing vortices which would retain airborne particles for long periods of time. Further demonstration might include a maximum purge-down time from, for example, GMP Grade D particle burden, down to the values given in the conjectural table above.

HEPA filtration of the air passing through an isolator is, of course, fundamental to operation, both for positive and negative pressure applications. Cleanroom standards do offer some guidance, but an isolator standard could be more specific. The need to fully test the supply filters on aseptic isolators, and the exhaust filters on containment isolators, is paramount. Our conjectural standard might specify correctly-sited and well-labelled DOP test ports, and it should place defined limits on the measured filter penetration, under test. Again, some discussion would be needed to set these values, involving filter manufacturers and isolator users. This issue really has to be addressed with absolute clarity in any isolator standard.

Where the application is both aseptic and toxic, as for example in the preparation of cytotoxic parenteral solutions, the ISO standards 14644 and 10648 are of limited use since neither cover this situation, and ISO DIS 13408-6 is technically not applicable.

Isolator operating pressure is generally viewed as a primary aspect of isolator function, although studies in the past have indicated that isolator pressure is actually not a critical parameter in achieving the required conditions. *Handling cytotoxic drugs in isolators in NHS pharmacies*[14] states: "As stated previously, there is much more to consider than merely the pressure differential of the system. If the above sources of exposure and product contamination[ii] can be minimised, then the type of system selected should be less important. This assumes that there is no catastrophic leakage. In this case, alarm systems and training systems become paramount." That said, an isolator standard might reasonably require that the isolator holds a sufficient pressure so that a positive pressure isolator cannot go negative during rapid glove withdrawal, and a negative pressure isolator cannot go positive during a rapid glove insertion. The standard might also promulgate a maximum time for return to set pressure after a given fluctuation. Beyond this, the standard might offer an acceptable range of pressures for positive pressure aseptic work, and for negative pressure toxic containment.

Leak rate is an issue which exercises isolator users considerably, and here the standards ISO 14644 Part 7 and ISO 10648 Part 2 do actually provide us with a choice of four classes of leak rate with which an isolator might conform. However, there is no guidance as to what class of leak rate is appropriate to what application and manufacturers still use leak rates other than those specified in these standards. Furthermore, there is very little guidance as to how the leak rate should actually be measured in practice: what test pressure should be applied, what should the length of time be for the test, what decay value is appropriate, and should changes in atmospheric pressure and isolator temperature be considered. A standard might offer a range of suitable tests, and the limits which would be applied.

Table 2 shows a suggested structure for isolator leak rate and application.

Table 2: Suggested isolator leak rates by application

ISO Class of Leak Rate	% Volume Loss per Hour	Application
1	0.05	Class 3 MSCs
2	0.25	Negative pressure aseptic isolators. High containment isolators.
3	1.00	Positive pressure aseptic isolators. Medium containment isolators.
4	10.0	Not applicable

ii. The factors specific to product contamination are listed in the preceding section of the document

In passing, EN 12298:1998[15] mentions the concept of BATNEEC (best available technology not entailing excessive cost) with regard to leak rates, but offers no further guidance. ISO DIS 13408-6 ducks the issue of leak rate and refers the reader to ISO 14644-7, which means yet again, the user has to sort through another document to find the appropriate information.

Some consideration might be given in an isolator standard to the issue of instrumentation and alarms. This is a topic which is singularly lacking in the otherwise quite comprehensive ISO DIS 13408-6. A relatively small isolator once reviewed by the author boasted over 400 separate alarms, of which the manufacturer declared over 80 as critical. Only five factors are critical to the general operation of an isolator:

1. HEPA filtered air-flow rate, either UDAF or turbulent. This is easily measured and alarmed.
2. Isolator pressure. Whilst isolator pressure does not seem to be critical as such, it is a strong indicator that the isolator is working as normal. For this reason, it should be standard practice to fit an alarm system on the isolator pressure gauge. Such an alarm might be arranged to operate on both high and low excursions from the values set by either the isolator manufacturer or the user.
3. Pressure drop across the main filter is often measured and alarmed.
4. HEPA filter integrity. This can only be measured during DOP testing and is not 'alarmable'.
5. Leak rate. This can only be measured by out-of-service methods and is also not 'alarmable'.

Thus, the only critical alarms on an isolator are, in practice, the air-flow rate, the pressure inside the isolator and the pressure drop across the main filter. Any standard should note this. Failures, other than HEPA filter integrity and leak rate, will show up as changes in these three parameters and therefore do not need to be alarmed as such. That said, it is comforting to have an indication of what item has failed, when an alarm does occur. For example, if the pressure in a pneumatic door seal were to drop below a set value, a message to this effect would allow rapid remedial action.

Various existing standards give an indication of the requirements for the bio-decontamination of aseptic isolators (e.g. BS EN 14937: 2001[16]), but again none are specific. ISO DIS 13408-6 alone provides quite good discussion of bio-decontamination, and is recommended as a useful guide. The application of hydrogen peroxide to the bio-decontamination of isolators perhaps merits a whole standard in its own right, however an isolator-specific standard might give some basic requirements for bio-decontamination. This could, for instance, list the demonstration of log 6 reduction of *G. stearothermophilus* spores, and aeration down to 1 ppm before opening the isolator, as primary bio-decontamination requirements.

Isolator room conditions would really have to be addressed by the proposed standard. In theory of course, room standards need not be high since the isolator, by definition, provides the required standard for the process. In reality, defined isolator room conditions are needed for setting up the open isolator, for cleaning, and for minimising the bio-burden on the isolator and its transfer systems. Leading on from this, a standard might indicate the minimum requirement for garments and gowning for given isolator applications and the room conditions.

On a personal and more general point, standards such as ISOs can be difficult to read and to interpret in a practical sense, even when numbers and values are provided. To some extent, this may stem from the fact that they are drafted by committees, often with varied cultural backgrounds and languages. This is apparent in ISO DIS 13408-6 which whilst containing much useful information, is illogically organised, and needlessly repetitive in places. Final editing by a native English speaker might be helpful in this respect.

Conclusions

Clearly, a standard for pharmaceutical isolators could be extended into a lengthy document including the many aspects of isolator design, construction and operation. As mentioned, the application of hydrogen peroxide vapour to bio-decontamination, could in itself be the subject of a standard. However, a practical and workable standard needs to be pared down to the basics for safe operation. It needs to lay down absolute requirements, but it also needs to offer a range of values or choices where appropriate. Both isolator manufacturers and isolator users are naturally keen to conform to standards, but standards tend to flag up various parameters, without providing applicable values or numbers. Clearly standards cannot be highly prescriptive, but the audience for isolator standards is quite desperate to see figures they can use in practice. Perhaps a set of guidelines in the format of a standard might be established in the first instance.

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The sense and otherwise of ISO 16890: Air filters for general ventilation

Alexander Fedotov and Oleg Provolovich

Abstract

At the end of 2016, the ISO 16890 series of standards replaced EN 779 standard on filters for general ventilation. EN 779 is well-known, well accepted and widely used for the specification of pre-filters for cleanrooms and other controlled environments. It was declared that ISO 16890 gives a better picture of indoor air quality than EN 779 in terms of particle contamination.

But is this really so?

There are two areas of application for air filters for general ventilation that differ from each other in principle:

- to protect humans
- to help achieve the necessary air cleanliness levels by serving as pre-filters in certain technologies and processes.

The first purpose has been known for centuries but the second came from industrial progress and the appearance of cleanrooms and other controlled environments. This article discusses this and other issues concerning ISO 16890.

Hygiene vs process

ISO 16890[1] was developed to provide better protection of humans who inhale over 25 000 000 particles with every breath and to replace EN 779.[2] The ideology is based on research of Swedish Prof. Svartengrens on Air Quality and Morbidity[3] and the relevant WHO report. His research is interesting but can it be a rationale for changing, even turning on its head, the whole international system of filter classification and testing, a system that has been well developed over decades and accepted in EU and many other countries? The main idea of ISO 16890 is to protect the human breathing system, not health as a whole. Surgery and intensive care units are not specifically covered. The introduction says "fine dust can be a serious health hazard, contributing to or even causing respiratory and cardiovascular diseases. Different classes of particulate matter can be defined according to the particle size range. The most important ones are PM_{10}, PM_5 and PM_1" However more than 50 % of the filter market relates to process needs. ISO 16890 pretends to be applicable everywhere, but is designed for hygiene purposes, ignoring the needs of processes.

Is ISO 16890 really useful for health protection? – No!

The human breathing system against particle contamination is not so simple. ISO 16890 is focused on protection against particles in outdoor air. But this air is deemed to be fresh in the majority of cases. Humans (as mammals generally) have always breathed outdoor air and are adapted for it. So normal air with its particles is a natural atmosphere for a human being. To make it cleaner is analogous to eliminating the 500 hundred different types of microorganism in a human body with total number of ca. 10^{14}.

We spend a lot of time in the street, in cars and in other environments, assuming outdoor air as fresh and healthy. Human evolution developed for all of us to survive in normal air. Where air is polluted with smoke in heavily industrial areas, it is quite enough to use the EN 779 filter classification.

What is ISO 16890 for?

- For residential premises? – hardly.
- For offices with the intention of pressing all of us to implement a new system? – Maybe but it is not necessary. We spend more than 2/3 of a day in environments where air filtration is barely needed. The rest, less than 1/3, is working time where process protection can be in use. It is important to know that HVAC for residential premises is the subject of special legislation that is under state control. There is no evidence that this fact was considered in ISO 16890.

Air deionization is another interesting issue. Some studies have found that fine filtration of particles < 1 µm causes air deionization.[4,5] There are ions in normal air and human evolution means that this natural ionization is not only harmless but is useful or even necessary for normal life. Removal of ions in the air can be risky. We accept breathing deionized air at our high-tech work places but why should we enforce this in our private lives?

Classification

EN 779:2012 specifies 9 filter classes for pre-filters:

- G1 – G4 – coarse filters;
- M5 – M5 – medium filters and
- F5 – F9 – fine filters.

This classification serves well both for general and cleanroom applications (as pre-filters). ISO 16890 classifies airborne particles for four categories: – PM_1; $PM_{2.5}$; PM_{10} and Coarse particles as shown in Table 1 and these categories are divided into 30 classes.

Table 1 ISO 16890 Filter categories

Filter main categories	Definition For PM_1, $PM_{2.5}$ and PM_{10} filters: Mass concentration of particles expressed in µg/m³ with aerodynamic diameter,
PM_1	< 1.0 µm
$PM_{2.5}$	< 2.5 µm
PM_{10}	< 10 µm

Mass vs number concentrations

EN 779 operated with particle concentrations by number for 0.4 µm particle size for filters M5 – F9. This allows for the easy calculation (estimate) of the total efficiency of a sequence of filters including HEPA and ULPA filters because the MPPS lies approximately between 0.3 – 0.5 µm.

However ISO 16890 uses particle concentrations by mass. This can be used for dirty premises but not for cleanrooms or other controlled environments where air cleanliness in terms of particles concentrations is of interest.

Particles sizes and ranges

Cleanroom philosophy is based on particle counts of particles ***larger*** than the limit specified, e.g. >0.5 µm or 5 µm. By comparison, ISO 16890 operates with measurement of mass particle concentrations of particles that are ***less*** than the particles size specified

Table 2 – Optical particle diameter size ranges for the definition of the efficiencies, ePMx

Efficiency	Size range, µm
ePM_{10}	$0,3 \le x \le 10$
$ePM_{2.5}$	$0,3 \le x \le 2,5$
ePM_{1}	$0,3 \le x \le 1$

The most common particles threshold for cleanrooms is 0.5 µm. High tech industries operate with 0.1 µm and other small thresholds. All this shows again that ISO 16890 is not for cleanrooms.

Design

It is declared that ISO 16890 provides better human protection and makes design and maintenance more effective. Let's see how it is done. At the design stage one selects the number of filter stages and the filter types. Industries and hospitals apply multi stage sequences of filters. For many years optimal schemes for selecting pre-filter classes were developed using EN 779. This allowed the transparent optimization of sequences of filters with different classes using a simple designation, e.g. M5; F7; F9. This is a practical engineering tool. ISO 16890 offers 30 filter classes. It is more complicated and not always clear. Which filter is better? The 2nd group with efficiency of 65% or the 3rd group with efficiency of 52%? A responsible answer can hardly be found considering the massive choice of combinations of particle size and concentration.

It is important to know that air filters for process represent more than 50% of the filter market. These are filters for hospitals (operating theatres, intensive care units), pharma and food factories, microelectronics, gas turbines and many others. The effect on human lungs has no relevance. Each of these areas has specific requirements and EN 779 helps to achieve them.

Changing of a well-established system without any justification will cause general confusion and possible disaster in practice. The new system will require specially trained people and their work will not be clear and transparent for many end-users and so will be risky. Therefore this new standard creates unacceptable risks for pharma and other responsible industries.

Is there any merit in specifying 30 filter classes? Air filtration is not a precise science. Particle concentration in air fluctuates day and night, from season to season etc. Therefore precise specification of filter classes is unnecessary, impractical and therefore pointless.

If it is assumed that the high precision of ISO 16890 is actually useful, then how does a designer select the appropriate class? No proper criteria are given in this standard. Some publications offer translations of EN 779 classes into ISO 16890 classes but these confirm that the whole story with ISO 16890 is a play with words without any benefits.

Testing

An important disadvantage of the new standard is that it only specifies testing of unloaded filters.

The initial pressure drops of filter groups 3-4 (ISO 16890) and F5-F9 (EN 779) are 100-120 Pa and final pressure drops 300 and 450 Pa respectively. Pressure drops increase due to filters soiling with dust and the mechanical forces then increase 4-8 times. Most filter materials have fibre structures that can stretch and thin resulting in a reduction of filtration efficiency. With ISO 16980, neither the filter manufacture nor the customer will see this. The EN 779 testing procedure requires step by step filter dusting and then checking the efficiency with particle counter at each step. This gives a true picture of filter function in actual use.

Conclusions

1. Changing the filter standard from EN 779 to ISO EN 1690 has no scientific or technical rationale and is more likely based on a compromise between EN 779 and ASCHRAE 52.2 and commercial interests.
2. ISO 16890 will be very misleading for designers and users who will not be able to understand it without external help.
3. ISO 16890 is a hygiene standard and does not consider specific requirements for process requirements which represent a significant proportion of applications.
4. The principle methodical approach has not changed and the necessary improvements could have been realized by a review of EN 779.
5. Absence of step-by step contamination of filter when testing does not allow users to have a true picture of a filter's operation during its whole service life.

Concluding observations

The background for ISO 16890 was the existence of two different standards for filters for general ventilation: EN 779 in Europe and ASHRAE 52.2[6] in the USA. It was decided that this was not good for global trade, so harmonization was required. A natural expectation was that this would result in a standard accepted by both parties. This has not occurred! The USA has not approved ISO 16890 and remains with ASHRAE 52.2! So this idea failed. Both the European and the American standards have been in use for decades and have satisfied the needs of users and manufacturers. They are equivalent in practice despite differences in classification and testing. Both USA and Europe produce excellent filters. So the differences in the original standards are not important and there was no necessity for trying to harmonise them.

The consequences of the exercise are that a strange and a very inconvenient standard has appeared that is not accepted by one side (USA) and has brought disruption to the other (EU, Russia and some other countries). It was not a compromise between two practices.

The new standard appeared because two big parties could not come to an agreement and possibly some people took advantage to promote their own goals. ISO 16890 has destroyed the well designed and accepted filter classification and testing system of EN 779. It gives no benefits for practice and is harmful for users in industry. Who has won? – Industries? – No! – Customers? – No!

So who? The answer might be found in the fact that ISO 16890 requires filter manufacturers to replace expensive filter testing equipment. Only large filter manufacturers can do this quickly and without too much trouble. Smaller companies who currently occupy a rather big part of the filter market will

be swept away in favor of large companies. All the propaganda about care for our health might have been aimed at achieving this marketing goal.

Is such a fundamental change of filter standards justified?

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Dr. Alexander Fedotov, graduated from St. Petersburg Institute of Communications in 1972 as engineer in automated systems. His has carried out scientific work on reliability and computer modeling of complex systems and has about 30 years of experience in cleanroom design, construction and testing. He is the author of three books *Cleanrooms* (1998; 2003), *Basics of GMP, Manufacturing of Sterile Medicinal Products* (2012) in Russian and of two chapters in *Cleanroom Management in Pharmaceuticals and Healthcare* (2013, Euromed) in English. He is currently Managing Director if a cleanroom design company, Invar-project Russia, and President of the Russian Association of Engineers for Microcontamination Control (ASENMCO).

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Dr. Oleg Provolovich, graduated from the Polytechnical Institute in Russia in 1985. He has extensive experience in research of aerosols and developing and manufacturing air filters. From 1992-2010 he was head of the 'Cleaning Air' scientific laboratory (Santhekh NII Project Institute, Moscow). Since 1995 he has been Technical Director of "NPP "FOLTER" LLC based in Moscow, a leading Russian manufacture of filters for general ventilation, HEPA filters and ULPA filters.

EN 1822 and EN ISO 29463

Chris Hews

A step towards a globally unified standard

In 2018, as a step towards a globally unified standard, CEN adopted Parts 2-5 of ISO 29463 (2011)[1,2,3,4] and reissued them as Parts 2-5 of EN ISO 29463 (2018).[5,6,7,8] At the same time CEN revised EN 1822-1:2009 to make specific reference to Parts 2-5 of ISO 29463 and reissued it as EN 1822:2019.[9]

EN 1822-1:2019 contains a standardised filter classification in terms of efficiency, both local and integral, and procedures for the determination of that efficiency on the basis of a particle counting method using a liquid, or alternatively a solid, test aerosol

Current, global, filter efficiency testing is based on the following two approaches:

1. In the US, IEST RP-CC001[10] specifies a thermally generated particle size of 0.3µm. A particle size of 0.3µm was selected as it reflected the size of the radionuclides of most concern within the nuclear industry. In classifying overall filter efficiencies, the US under IEST RP-CC001, along with other non-European countries, implemented the practice of using whole decimal percentage numbers: 99%, 99.9%, 99.99% etc. along with local permissible leak values.
2. In Europe, EN 1822 determines the efficiency of a filter at its Most Penetrating Particle Size (MPPS) (0.12-0.15µm for glass media) and states integral and local values that must be met in order to achieve a specific filter class. The efficiency of filters is then defined through the use of half decimal percentages: 99.95%, 99.995% etc..

The retention of EN 1822-1:2019 has three key aspects:

1. It reflects a view amongst CEN member countries that standardising on filter testing to the most penetrating particle size (MPPS) with an optical particle counter is the preferred and more reliable method for a filter manufacturer to determine the 'true' efficiency of a filter.
2. The existing E10-U17 filter classifications under EN 1822-Part 1 remain and would appear to reflect an agreement amongst CEN member countries that the amalgamation of the eleven classifications from IEST RP-CC001 and the eight from EN 1822 into thirteen new ISO classes within ISO 29463 Part 1 would be too complex and confusing.
3. Aerosol photometers are not specified for manufacturers' factory filter efficiency testing but of course remain widely specified for in situ testing of installed filters under ISO 14644-3:2019.

Parts 2-5 of ISO 29463 are heavily derived from the corresponding EN 1822 Parts but include some changes to meet the requests of non-EU members to address the lack of equivalence and divergent approaches to filter efficiency testing and classification across the world.

References

1. ISO 29463-2:2011 – *High-efficiency filters and filter media for removing particles in air – Part 2: Aerosol production, measuring equipment and particle-counting statistics.* International Organization for Standardization, Geneva. 2011.
2. ISO 29463-3:2011 – *High-efficiency filters and filter media for removing particles in air – Part 3: Testing flat sheet filter media.* International Organization for Standardization, Geneva. 2011.
3. ISO 29463-4:2011 – *High-efficiency filters and filter media for removing particles in air – Part 4: Test method for determining leakage of filter elements-Scan method.* International Organization for Standardization, Geneva. 2011.
4. ISO 29463-5:2011 – *High-efficiency filters and filter media for removing particles in air – Part 5: Test method for filter elements.* International Organization for Standardization, Geneva. 2011.
5. EN ISO 29463-2:2018 – *High-efficiency filters and filter media for removing particles in air. Part 2: Aerosol production, measuring equipment and particle-counting statistics.* CEN. 2018.
6. EN ISO 29463-3:2018 – *High-efficiency filters and filter media for removing particles in air. Part 3: Testing flat sheet filter media.* CEN.2018.
7. EN ISO 29463-4:2018 – *High-efficiency filters and filter media for removing particles in air. Part 4 Test method for determining leakage of filter elements.* Scan method. CEN. 2018.
8. EN ISO 29463-5:2018 – *High-efficiency filters and filter media for removing particles in air. Part 5 Test method for filter elements.* CEN. 2018.
9. EN 1822-1:2019 – *High efficiency air filters (EPA, HEPA and ULPA). Part 1: Classification, performance testing, marking.* CEN. 2019.
10. IEST RP-CC001.6: *HEPA and ULPA Filters.* IEST.

Chris Hews currently has a business development role at Camfil Limited. He has worked within the Clean Air industry for 27 years for a variety of specialist companies from consultants through to specialist cleanroom and regulated facility equipment manufacturers. He has held management roles within strategic development, technical sales, marketing and market management both nationally and internationally and has presented and trained to global audiences in Europe, Asia and the US.

Cleanrooms – known unknowns: 1. Source strength

Andrew Watson

Abstract

This article is the first of a series that identifies gaps that still exist between practice and meaningful verification in the design, operation and testing of cleanrooms. The topic for this article is source strength and the article assesses the validity of published source strength data as well as source strength data derived from body box testing for the purpose of calculating airflow rates in cleanrooms.

Introduction

Cleanrooms have been with us in a formal sense for over 50 years now. With 50 years of development, research and refinement, you would expect that by now we are designing facilities that accurately deliver to the brief. That brief requires that they behave exactly as intended, fully under control and within the expectations of the client. Generally, we do design to the brief, but rarely with absolute confidence. To give ourselves the best chance, we over-design, under-qualify and generally muddle along hoping that everything will be alright.

The over-design and under-qualification covers for what are fundamentally short-comings in our knowledge; things that Donald Rumsfeld famously qualified as "known unknowns". Nominating a particular cleanroom-based unexplained behaviour as a "known unknown" is risky, as there may well be an expert out there that knows exactly why things happened the way they did. To them, your "known unknown" is a "known known".

In reality, our known unknowns are a spectrum; sometimes we know a lot and we can make an educated guess, with little risk. Sometimes we know very little, but convention, expectation or myth forces us to make a decision that is little more than a leap in the dark. When it comes to verification our test criteria are often vague, or consist of activities that provide little data of relevance. We skew our activities to achieve certain results and sometimes we even ignore apparent outliers that are actually a signal that something is not completely right.

Known unknowns in context

As discussed above, Donald Rumsfeld's interpretation of known unknowns, during a news briefing on evidence of weapons of mass destruction in 2002, brought the term into ubiquity. In its full context:

> *"Reports that say that something hasn't happened are always interesting to me, because as we know, there are known knowns; there are things we know we know. We also know there are known unknowns; that is to say we know there are some things we do not know. But there are also unknown unknowns—the ones we don't know we don't know. And if one looks throughout the history of our country and other free countries, it is the latter category that tend to be the difficult ones."* [i]

However, this was not the first instance. Back in 1979, in evidence provided on risks with uranium mining, the great geotechnical engineer Dr Elio D'Appolonia provided a more technical (and better worded) description of known unknowns.

> *"Known unknowns result from recognized but poorly understood phenomena. On the other hand, unknown unknowns are phenomena which cannot be expected because there has been no prior experience or theoretical basis for expecting the phenomena."* [ii]

The engineering and scientific-based principles that govern the operation of a cleanroom, I would argue, are well understood. The translation to readily observable data, I would argue, is not. The gaps between the theoretical and the observed need to be identified and addressed if we are going to improve the design, construction, verification and operation of cleanrooms. Already we are seeing a response to the gap, with a plethora of emerging technologies for cleanrooms, contained areas and specialist laboratories that promise to provide certain conditions, but lack the ability to verify their effectiveness on installation or at a later point in the life-cycle. This is a direct result of the ignored known unknowns.

This article is to be the first in a series of articles that seek to identify the known unknowns in cleanroom technology. Hopefully these articles will provide the impetus to bring these

i. DoD News Briefing – Secretary Rumsfeld and Gen. Myers, Presenter: Secretary of Defense Donald H. Rumsfeld, February 12, 2002 11:30 AM EDT

ii. Proceedings of the British Columbia Royal Commission into Uranium Mining (D'Appolonia, 1979)

known unknowns into the realm of the known knowns. Perhaps a few unknown unknowns will be stumbled upon along the way that will drive our knowledge even further.

Source strength

The new ISO standards that have recently been released or are under development will bring the research of the past 30 years to the forefront of cleanroom design. We are now developing a revision of ISO 14644-4[1] that brings into question current basic rules of thumb such as percent ceiling HEPA coverage or air change rates in favour of a new, more science-based approach. The implementation is fairly straight-forward, but the success of the implementation is limited by the quality of the data available.

During the review of ISO 14644 Part 4 and the preparation of the Energy efficiency standard ISO 14644 Part 16,[2] much time and effort was devoted to the preparation and rationalisation of the equations used to determine an appropriate air supply rate. Throughout this process we were very aware of a significant known unknown – the actual source strength values, or estimated particle emission rates for equipment and personnel that would be used with these equations. There is a range of published values. However the measured data vary widely both from paper to paper and sometimes even within a single paper. For a single item of equipment variation of several orders of magnitude was observed. Similarly, for personnel, huge ranges of particle emission rates were found amongst the general population.

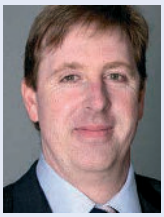
There was some discussion that we should introduce some of the published data into the ISO standards. However it was assumed that better data would become available in the future. In addition to this, when the published source strength data was broken down by particle size some experts noted that the distribution did not necessarily reflect the distribution between ISO classes and particle size as shown in the table of ISO Classes of air cleanliness by particle concentration ISO 14644-1.[3] (This was despite the statement in the standard that "Particle number concentrations for different threshold sizes in Table 1 do not reflect actual particle size and number distribution in the air and serve as criteria for classification only." In any event there were wide variations in calculated air supply rates when different particle sized source strengths were used in the equations.

A deeper dive into the origins of the published data revealed another complication. Most, if not all the published data looked at the total particles shed, as measured using a body box. In a body box, the particle counter is located in the air stream that is removed at low level so as to pick up all the particles shed. However, for classification purposes, ISO 14644-1 (A.4.2.d) requires the particle counter probe to be placed "in the plane of the work activity." Typically, this will be at approximately 0.9 to 1.2 metres above floor level. Therefore, the source strength, as measured using a body box, is likely to be overstated for the purpose of calculating the air supply rate required for a particular cleanliness class. This is particularly so for larger particles that tend to settle quickly. There are further limitations on these methods that are a result of inadequate testing practices, particularly when it comes to activities performed during "in operation" facility certification and monitoring.

References

1. International Organization for Standardization. ISO 14644-4:2001 – Cleanrooms and associated controlled environments – Part 4: Design, construction and start-up. Geneva 2001.
2. International Organization for Standardization. ISO 14644-16:2015 – Cleanrooms and associated controlled environments – Part 16: Energy efficiency in cleanrooms and separative devices. Geneva 2015
3. International Organization for Standardization. ISO 14644-1:2015 – Cleanrooms and associated controlled environments – Part 1: Classification of air cleanliness by particle concentration. Geneva 2015.

Author's note: For the next few issues I intend to explore further the "known unknowns" in the field of cleanroom design and operation. The material will be drawn from my own experiences and other experts with far more experience than my own. As part of the preparation of these future articles I would value your feedback and your own experiences. Of course, as we are discussing issues at the boundaries of our understanding, I am always ready to receive corrections, comments and additional research material. Andrew Watson.



Andrew Watson is a Director of CBE, Centre for Biopharmaceutical Excellence, Australia. He is a Bachelor of Engineering (Chemical and has 25 years' experience in the design, construction, commissioning/validation and operation of a wide range of high tech facilities, including pharmaceutical manufacturing, high containment, industrial cleanroom, hospital pharmacy and specialist research facilities. This experience extends to facility layout, building fabric design, construction, and HVAC, utility and purified water specification. His project management experience encompasses all aspects of FDA, EU, TGA, PIC/S and associated regulations, local and international standards and general quality practices. He has performed gap analyses on many pharmaceutical manufacturing facilities and sterile/cytotoxic dispensing suites to assess aspects of compliance, safety, design and rectification. Andrew is a past president of ISPE (Australasia) and is active in establishing ISO standards. He is Independent Chair of ME-060 (Cleanroom Standards) for Standards Australia and a committee member for ISO TC-209 – (ISO 14644 and 14698 suite of standards).

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Decontaminating and decommissioning a biological containment facility

John Yuill

Abstract

This article is aimed at giving a greater understanding of the requirements of decontaminating and decommissioning equipment and facilities that have been contaminated with products that could adversely affect the health and well-being of the decontamination operatives involved in its safe removal. The article also discusses the effects on the environment and other staff along the safe disposal routes of the resultant wastes produced.

Successful decontamination and decommissioning

Decontamination and decommissioning of a facility used for pharmaceutical research and manufacture of APIs (active pharmaceutical ingredients) is generally straightforward, depending upon the equipment and the contaminant, as long as historical information, correct procedures and a trained and experienced team are available.

Decontaminating and decommissioning a biological containment facility can be a very different story due the level of risk of exposure to pathogens, viruses, bacteria, or toxins for the decommissioning operatives, the surrounding areas and even beyond.

This work demands a much higher level of precautionary control and protection, and a very well trained and managed team who are used to and specifically trained for this type of work.

Nothing must go wrong with these precautionary and protective measures during the course of the work as failure in any part of the system would lead to catastrophic consequences for those involved in the work as well as those involved in the route to disposal.

The author first became involved with a decommissioning project of a biological containment facility in the early 1990s at a specialist pharmaceutical and laboratory facility in South Wales.

In this facility potentially harmful cytotoxins as well as many other active pharmaceutical products were being manufactured in one area and hormonal products in another. Members of the team had to be completely separated from the environment of the suite by means of positive pressure air suits controlled by strict procedures. There was risk and danger to the manufacturing team and the public but not on the scale of risk that would arise if a high-consequence pathogen were released into the environment, where the resultant consequences would be immediately devastating.

Once all the internal equipment had been decontaminated it was found in one of the production facilities that all wall, ceiling and floor coverings were also contaminated. These had to be removed and disposed of by incineration, as product was found to have been absorbed into surfaces and could not be removed or neutralised.

Following this project experience was gained in decontaminating and decommissioning numerous API areas in pharmaceutical complexes in the UK and Europe, down to levels as low as 0.05 µg/100 cm^2! In addition, other more higher-risk biological areas and facilities were investigated and then decontaminated.

These new areas presented a much higher risk from certain pathogens that posed an immediate danger to the decontamination operatives, the client, the public and the environment.

Having researched the products involved and the possible effects of exposure, the conclusion was quickly reached that the magnitude of precautionary measures would need to be greatly increased. These would start with swabbing and analysis followed by cleaning, stripping down and safe disposal or incineration under specifically written, strictly controlled and carefully managed procedures.

Proper preparation is absolutely essential when the possible pathogens might include anthrax, SARS , tuberculosis, typhus, yellow fever, malaria, Bolivian haemorrhagic fever, Marburg virus, Ebola virus, Lassa fever virus, Crimean–Congo haemorrhagic fever, or Variola virus (smallpox) etc..

Each facility had to be treated as unique with its own requirements, risks and dangers. It was not sufficient to use a generic risk assessment. The work from start to finish had to be very carefully analysed and planned and then agreed with the client's Health, Safety and Environment Department.

Sufficient time had to be allowed for a comprehensive scoping exercise to effectively investigate the historical information of the facility so that planning could include:

- The methods to be used, the risks to be expected, the equipment required and safe disposal routes to be identified for contaminated waste materials:
- The monitoring plan for swabbing and analysis which would prove success and ensure the elimination of exposure for all involved, including the environment and the public at large.

Many post investigations for clients have shown that associated ventilation and extraction equipment was missed, so it is vitally important that the whole of the utilities support systems equipment is included in the scoping work.

John Yuill is the senior Technical Director of RCS Pharma. RCS Pharma specialises in decommissioning and decontamination of pharmaceutical equipment, facilities and areas. John has over 40 years' experience in environmental engineering, decommissioning and decontamination with comprehensive knowledge having worked on oil, gas, petrochemical, pharmaceutical and nuclear facilities. He is involved with, tenders, work scope, contracts and project management of operational projects.

Observing airflows in cleanrooms

Bill Whyte

Sir

I have recently been involved in discussions about methods of observing airflow in cleanrooms by the use of threads, film tapes, or cloth, according to the method published in the new ISO 14644-3.

Several years ago I used various threads and streamers to observe airflow in cleanrooms. It became obvious that they did not show the correct airflow direction. I reported that 'streamers will indicate the direction of airflow but, because of their weight, they do not flow exactly in the same direction as the air. This is a problem that increases as the air velocity decreases and weight of the streamer material increases. A horizontal flow of air with a velocity of about 0.5 m/s is required to get a typical streamer to stream at only 45% to the horizontal, and a velocity of about 1 m/s for it to stream almost horizontally i.e. in line with the air stream.'

I would not use threads and steamers to study airflow but many people do. If they do, they should be aware of the problem that exists and use the best material available. Threads are best and FlowViz, which is light multi-stranded mono-filament nylon thread, is a good example of a suitable material. It is available from M&A in the USA (www.dmilholland.com/floviz).

Yours sincerely

Bill Whyte
School of Engineering,
University of Glasgow,
Glasgow G12 8QQ

'FlowViz' nylon thread streamer on an anemometer

Life-lines

Quotations of Napoleon Bonaparte

Great ambition is the passion of a great character. Those endowed with it may perform very good or very bad acts. All depends on the principles which direct them.

A leader is a dealer in hope.

The battlefield is a scene of constant chaos. The winner will be the one who controls that chaos, both his own and the enemies.

The people to fear are not those who disagree with you, but those who disagree with you and are too cowardly to let you know.

Never interrupt your enemy when he is making a mistake.

One must change one's tactics every ten years if one wishes to maintain one's superiority.

Impossible is a word to be found only in the dictionary of fools.

Nothing is more difficult, and therefore more precious, than to be able to decide.

Take time to deliberate, but when the time for action has arrived, stop thinking and go in.

There is one kind of robber whom the law does not strike at, and who steals what is most precious to men: time.

References from Editorial on page 3

1. *Global guidelines for the prevention of surgical site infection*. World Health Organization. World Health Organization, Geneva, Switzerland, 2016.
2. Whyte W, Lytsy B. *Ultraclean air systems and the claim that laminar airflow systems fail to prevent deep infections after total joint arthroplasty*. Journal of Hospital Infection 2019. 103 (1): 9-13.
3. Sharp J. *Massacre of the Innocents*. European Journal of Parenteral & Pharmaceutical 2006. Volume 11 Number 4: Editorial.

New SAS Tri-Clover Isolator Head available from Cherwell Laboratories

Cherwell Laboratories are delighted to announce the addition of the SAS Tri-Clover Isolator Head to their extensive range of air samplers for a broad range of environmental monitoring applications in cleanroom, isolator and other controlled areas.

The new SAS Isolator sampling head with tri-clover fitting is used in conjunction with the SAS Super Isolator which offers an extremely accurate, reliable and flexible monitoring solution for isolator cabinets and filling lines. Using bespoke sampling heads, these viable samplers can help reduce contamination of aseptic transfers during environmental monitoring procedures.

Allowing easier installation within RABs and filling lines, the new version has the same features as the standard SAS head but allows it to be more easily located in situ. Using an industry standard tri-clover (tri-clamp) fitting provides easy integration within confined spaces, as well as allowing quick and easy removal for service and/or calibration. The new sampling head can be supplied for Contact plates or Petri dishes.

For more information about Cherwell Laboratories, please visit www.cherwell-labs.co.uk.

New SAS Tri-Clover Isolator Head, Cherwell Laboratories

Ecolab introduces Validex harmonized global disinfectant efficacy test

Disinfectant efficacy testing can be a daunting task as there are numerous factors to consider with a number of standardized test methods available.

However, there are currently differences between the methods generally used in the EU and the US and all existing standards have individual pitfalls and unique challenges.

It is important to note that the existing standards are not specifically for cleanroom disinfectants and so adaptations to reflect a cleanroom environment should be considered with the support of guidance documents such as (USP) 40-NF35 Chapter <1072>.

All these factors have been taken into consideration and resulted in the Validex harmonized method developed by Ecolab to support efficacy studies conducted by end users. Further supporting data is also available on the performance of Ecolab disinfectants on a range of typical surfaces and isolates relevant to the cleanroom environment.

This additional supporting information serves as an extension of end users' own validation data, therefore minimizing the cost and resources required for their efficacy studies. This harmonized 'One Method' can give companies a transferable platform to achieve replicable results between laboratories and countries.

For further information on how Ecolab's Global Technical Consultants can help you reduce complexity and gain greater efficiency in your disinfectant efficacy validation processes. Contact Emily Buck on +44 (0) 1639 825 681 or email emily.buck@ecolab.com or visit www.ecolablifesciences.com

Envair Limited supplies custom built cabinets for B Braun

Envair Limited has recently completed a contract for the supply of custom-built horizontal UDAF cabinets for a Compounding Aseptic Production (CAPS) facility at B Braun Medical.

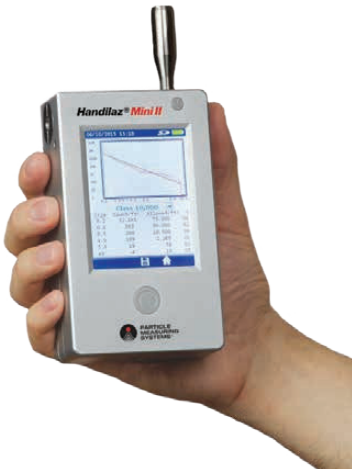
Working closely with the client, Envair designed these cabinets to provide additional length and depth of the internal work surface in order to accommodate specialist filling equipment.

UVC germicidal technology was also incorporated to complement the standard manual disinfection.

The expanded facility will allow B Braun Medical to develop the provision of its aseptic products across the UK.

For further information please contact info@envair.co.uk or visit www.envair.co.uk

Particle Measuring Systems releases the HandiLaz Mini II measuring down to 0.2µm



December 9th, 2019, Boulder, CO – For convenient and extensive point of use monitoring, the Particle Measuring Systems HandiLaz Mini II is a new low cost, handheld solution for cleanroom environmental research and troubleshooting needs.

The HandiLaz Mini II is uniquely suited for applications including semiconductor component and equipment manufacturing, wafer fabrication, advanced materials production and research and testing laboratories. This compact unit offers an unlimited number of particulate size channels from 0.2-10 µm with 10 nm channel resolution. It utilizes a miniaturized, state of the art sensor with a simple touchscreen, single button operation and advanced on-screen analysis for getting physically close to and in detail with cleanroom environments. Features include ISO classification, on-board temperature and relative humidity measurement, PM2.5 and PM10 analysis, embedded flow meter, and continuous particle logging through the integration of temperature and differential pressure input into the particle measurement for enhanced analysis.

Adding the HandiLaz Mini II to an environmental monitoring toolbox provides the benefit of advanced environmental monitoring in a highly compact package.

For more information visit www.pmeasuring.com/products/particle-counters-air-and-gas/handilaz-mini-ii-handheld-airborne-particle-counter/ or contact nmorton@pmeasuring.com

Record breaking numbers for Lab Innovations 2019 and The Cleanroom Hub

Lab Innovations celebrated its 8th edition on 30 & 31 October 2019, beating all records for the event. Attracting 3,860 attendees - an impressive 24% increase on the previous year - this makes it the largest Lab Innovations to date. Over 160 exhibitors displayed a diverse and innovative product offering to visitors from more sectors than ever before, emphasising the event's place as the UK's largest annual trade exhibition dedicated to the entire laboratory industry.

The Cleanroom Hub provided visitors with CPD accredited education covering hot topics from cleanroom monitoring and selecting the right garments, to the impact of EU Biocidal regulations and microbial aspects of water quality in controlled environments.

Cleanroom suppliers including Contained Air Solutions, CTS Europe, Felcon, Guardtech Cleanrooms, Esco GB, Monmouth, Shield Scientific, Gerflor, Helapet, Crowthorne, Wickham Laboratories, STERIS Life Sciences, Connect 2 Cleanrooms, Teknomek, Contec and more showcased cleanroom equipment to the UK's leading laboratory and cleanroom decision makers.

With new technological developments and digitisation expanding the boundaries of research and science, the popular Insights and Innovation seminars supported lab professionals in future-proofing their laboratory and learning best practice for lab management. Expert speakers demonstrated new technologies that will help accelerate or improve processes, benefit research and keep their laboratory at the forefront of the industry.

Lab Innovations 2020 will take place on 4 & 5 November at the NEC, Birmingham, UK. Register your interest to exhibit or visit on the event website: www.lab-innovations.com

Pinpoint secures new investment from Cherwell to develop ImpactAir Range

Pinpoint Scientific, manufacturers of environmental monitoring solutions for pharmaceutical and related industries, is pleased to announce it has secured further investment, to aid the development of its ImpactAir® range.

Cherwell Laboratories and Development Bank of Wales have both invested. This not only secures jobs in South Wales, but also allows the business to launch some exciting new products within the ImpactAir range. Cherwell is an existing distributor of ImpactAir products within the UK.

ImpactAir is designed for continuous monitoring in high-grade areas, where in-process sampling of viable particles is critical. The new ImpactAir® ISO-90 Monitoring Platform will shortly be added to the range. This modular system integrates into isolators or RABS in any orientation, using standard or custom-made connections. The ISO-90-Monitoring Head features a chamber for 90mm agar plates and slit to agar sampling. The low D50 value and ability to sample for long periods makes the ISO-90 ideal for continuous monitoring as demanded by the Annex 1 revision.

For more information please visit www.pinpointscientific.com or www.cherwell-labs.co.uk

Particle Measuring Systems announces distribution agreement with BD

December 6, 2019 – Particle Measuring Systems (PMS) recently announced a distribution agreement with BD (Becton, Dickinson and company) (NYSE: BDX), giving the medical technology company non-exclusive rights to distribute Particle Measuring Systems' MiniCapt® Mobiles and BioCapt® Stainless Steel Impactors globally. Per this agreement, BD will sell the instruments together with BD prepared plated media through their distribution network, and PMS will provide service and calibration.

"This agreement marks a milestone in our strategy to increase our footprint in the microbiology market and is a continuation in our strategy to partner with high quality companies who complement our product line," said Giovanni Scialo, vice president Life Sciences for Particle Measuring Systems.

This agreement provides customers with a complete portfolio of active air monitoring systems and high-quality prepared plated media to meet their environmental monitoring needs and regulatory requirements.

Particle Measuring Systems Inc. (PMS), a subsidiary of Spectris plc, is a global technology leader in contamination monitoring, the inventor of laser particle counting, and is now the leading provider of solutions for monitoring and controlling many forms of contamination that impact companies that manufacture in ultra-clean environments.

For more information on PMS, visit www.pmeasuring.com or contact nmorton@pmeasuring.com

RSSL starts 2020 with winter training offer

To help kick start your new year, Reading Scientific Services Ltd (RSSL) have launched their Winter training offer, providing a 20% discount on a selection of pharmaceutical training courses running from January – March 2020.

To take advantage of this offer simply book your training course by 31st January 2020 quoting the special offer code WINTER.

This offer is valid a selection of courses including:

- Biologically Derived Products - Testing and Manufacturing Challenges
- Technology Transfer
- Active Pharmaceutical Ingredients Auditing
- Good Manufacturing Practice - The Essentials
- Introduction to Validation
- Cleaning Validation with Swabbing Workshop
- Introduction to Pharmaceutical Microbiology
- Data Integrity & Electronic Records and Signatures

To view the full list of courses and to book your place visit: www.rssl.com/pharmaceutical-training/special-offers

An externally accredited training organisation (IRCA, RSC), RSSL provides a wide range of specialist courses delivered by a team of experts.

For more information please contact enquiries@rssl.com or call +44 (0)118 9184 076.

RSSL launches sterility testing service

Following sustained client demand and the opening of their state-of-the-art microbiology laboratory earlier in the year, Reading Scientific Services Ltd (RSSL) has launched a fast, responsive and flexible sterility testing service.

The move enables the award-winning Contract Research Organisation (CRO) to build on their diverse range of services, providing a compelling service offering - particularly for clients who are keen to work with just one trusted laboratory.

In addition to a standard 21 day turnaround, we are also offering clients an expedited 16-day and 14-day timeframe for sterility testing – one of the quickest available on the market.

To mark the launch of the new service, RSSL are offering an exclusive cost-saving offer to every client who engages their sterility testing services in the first 12 months and extending out an open invitation to pharmaceutical companies to visit our new facilities and discuss your testing needs.

To learn more please contact the RSSL team via enquiries@rssl.com or 0118 918 4076 or visit www.rssl.com

Contamination Control Everywhere in Our Lives

ISCC comes to Turkey

The 25th edition of the ISCC International Contamination Control Symposium will be held in Antalya hosted by the Cleanroom Technologies Society of Turkey.

Participate in the symposium while getting closely acquainted with Turkish culture and hospitality.

Enjoy the beautiful city of Antalya. Visit Düden Waterfalls, go to see Aspendos Theatre and swim on Belek Beach.

Get to know the unique gastronomy of this fascinating geography.

We welcome all contamination professionals and experts to share their knowledge and meet their colleagues from 13-15 October of 2020 in Antalya.
For more information please see is https://www.iscc2020.com/

Events

2020	Event	Organiser
April 1-2	PHSS Aseptic Processing Workshop Syndicates 2020, Manchester, UK	PHSS
April 27-30	ESTECH, Minniapolis/St.Paul, Minnesota	IEST
May 25-27	51st R3Nordic Symposium in Cleanroom Technology & Contamination Control, Naantali Spa, Finland	R3Nordic
June 2-3	Cleanroom Technology Conference 2020, Birmingham, UK	HPCi Media
June 2-3	Manufacturing Chemist Live 2020, Birmingham, UK	HPCi Media
June 22-24	EP and Clean Tech China, Shanghai, China	Informa Markets Sinoexpo
August 16-18	Cleanroom Guangzhou,2020, Guangzhou (Canton), China	Guangdong Grandeur International Exhibition Group
November 4-5	Lab Innovations, Birmingham, UK	Easyfairs
November 17-19	International Congress A3P, Biarritz, France	A3P
November 18-19	Cleanzone, Frankfurt, Germany	Messe Frankfurt Exhibition GmbH
November 24-25	Cleanroom Technology Conference 2020, Hyderabad, India	HPCi Media
December 1-2	Cleanroom Technology Conference 2020, Singapore	HPCi Media

Training courses

IEST (Institute of Environmental Sciences and Technology) www.iest.org		
2020	**Event**	**Location**
February 25	Understanding the Cornerstone Cleanroom Standards: ISO 14644-1 and 14644-2	Phoenix, Arizona
February 26	Application of ISO 14644-3	Phoenix, Arizona
February 27	Universal Cleanroom Operations Guidelines with ISO 14644-5	Phoenix, Arizona
April 27	Basics of Cleanroom Design, HVAC System Design, and Engineering Fundamentals	Minneapolis/St. Paul, Minnesota
April 28	Cleanroom Basics: What is a Cleanroom and How Does it Work?	ESTECH Minneapolis/St. Paul, Minnesota
April 29	Beyond Cleanroom Basics: Fundamental Information for Cleanroom Operations	ESTECH Minneapolis/St. Paul, Minnesota
April 30	Cleanroom Classification Testing and Monitoring	ESTECH Minneapolis/St. Paul, Minnesota

CCN (Contamination Control Network) www.theccnetwork.org		
2020	**Event**	**Location**
May 19-21	CTCB-I Testing and certification course	Liphook, England

ICS (Irish Cleanroom Society) www.cleanrooms-ireland.ie		
2020	**Event**	**Location**
February 25	CTCB-I Cleanroom Testing & Certification, 2/3 days	Dublin. Ireland
September 24	CTCB-I Advanced Cleanroom Technology course, 1 day	Dublin. Ireland
November 26	CTCB-I Cleanroom Testing & Certification, 2/3 days	Dublin. Ireland

R3Nordic (Scottish Society for Contamination Control) www.r3nordic.org		
2020	**Event**	**Location**
For courses run by R3Nordic see https://r3nordic.org/		

VCCN (Association of Contamination Control Netherlands)		
2019	**Event**	**Location**
For a complete list of courses including CTCB-I courses, please see http://www.vccn.nl/cursusaanbod		

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

ONE METHOD

VALIDEX™ PROGRAM

In the absence of a single global standard for the validation of disinfectant efficacy in pharmaceutical cleanrooms, we have consulted with renowned industry experts to create one.

The Ecolab One Method Validex Program provides 'clear, sensible and reproducible criteria'[1] for the evaluation of disinfectants for use in pharma cleanrooms.

It provides a method and acceptance criteria appropriate to the industry globally, alongside a comprehensive data set on relevant cleanroom microflora and surfaces.

With the Validex Program our Global Technical Consultants can help customers navigate through disinfectant efficacy testing, with accredited laboratories. This helps you meet current regulatory expectations and, more importantly, comply with the standards required for cleanroom decontamination.

The Validex approach reduces complexity and helps you gain greater efficiency by giving specific guidance around validation processes.

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1. Sandle, T (2019) *Leading the Way to a Harmonised Global Disinfectant Standard,* Cleanroom Technology November 2019

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