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Enhance your knowledge of contamination control

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ENVAIR TECHNOLOGY
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Picture: Envair Technology's CDC F negative pressure cytotoxic isolator

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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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Contents

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Editorial

Welcome to CACR43!

I strive for a varied content in each issue so that there is something of interest for everybody. This time we start with a joint article by Tim Coles of Pharminox Isolation and Sanna Lehtinen of Vaisala on how vapour phase hydrogen peroxide bio-decontamination cycles can be better controlled using Vaisala's new sensor. This can give significant benefits which are described in the article.

The second article, by Hasim Solmaz, is on the subject of environmental monitoring in GMP-compliant laboratories. This is written in FAQ format which is perhaps a good way of providing most of the basic information that readers are interested in. The next in the 'known unknowns' series by Andrew Watson examines and questions the logic behind cleanroom airlocks. He concludes that in many cases, cleanroom layouts can be over-complicated … but will regulators agree?

The final main feature, by Tim Sandle, is about the risks of using ineffective hand sanitisers in cleanrooms. Hand sanitisers are now omnipresent in our everyday life, so much of what Tim writes about applies outside the cleanroom too. The risks are not just that some hand sanitisers are ineffective; they can be dangerous too!

Readers interested in an objective survey of where we are up to with coronavirus, and especially masks, immunization and rapid viral tests, should look at the latest blog from Imagine MD – https://imaginemd.net/blog/coronavirus-august-2020-part-9-masks-vaccines-and-rapid-testing/?fbclid=IwAR3kX_nZjxjW4kmjYCJuWLqmKw-hKpHj-n_LzHjG6cX4BZggLCl2f7sTW4E.

As might be expected, several of the commercial stories in the News section also concern coronavirus, from the logistics for service providers attending distant sites during the pandemic, to remote access to particle counter data from anywhere in the world. There is a nice cartoon with the latter! In fact humour can be a very good way of putting points across and I am always on the look-out for relevant cartoons to spice things up a bit. All contributions welcome.

Eleven years ago, when I was planning the very first issues of CACR, I had a few ideas up my sleeve that I thought would make interesting topics. The first of these was the history of microbiological safety cabinets and I was lucky enough to get Professor Raymond Clark to write a four part series spread over the first four issues. Another topic that I was keen to explore was particle fall-out in sampling tubes and Tim Russell of TSI developed some interesting calculations in the very first issue. I had been rather pleased with myself about a Venn diagram that I devised in my time at Envair to illustrate the interrelationships between the various clean air and containment products and different types of contaminant. This is shown in issue 3. Also in my previous life, I had been involved in promoting what I thought (and still think) was a very clever and yet simple zoned ultra clean air operating theatre so I wrote that up in issue 6. Finally I would like to record my gratitude to Bill Whyte. It was he who introduced me to the business of editing and to my publisher Euromed. In fact, more than anybody, he is responsible for my fulfilling second career as an editor. He has also been a major contributor to CACR, starting with an article on the measurement of air supply volumes and velocities in cleanrooms in CACR5, and he has provided many suggestions and contacts. All this helped to get CACR off to a good start, and technical articles have continued to flow since – from all my greatly appreciated authors!

John Neiger

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Real-time optimisation of vapour phase hydrogen peroxide bio-decontamination cycles using a new combined sensor

Tim Coles and Sanna Lehtinen

Abstract

Bio-decontamination cycles using hydrogen peroxide vapour are currently controlled parametrically. A new hydrogen peroxide sensor introduced by Vaisala gives real-time values for both peroxide concentration and relative saturation (the point at which water and hydrogen peroxide vapour condense simultaneously). This offers the opportunity to control gassing cycles directly, and thus the potential to develop more precise cycles with faster turn-around, and reduced de-gassing effects.

Introduction

Until recently, vapour phase hydrogen peroxide (VPHP) bio-decontamination cycles have been parametrically controlled, in most cases. The critical control parameters are the air/vapour flow rate, and the peroxide solution delivery rate to the evaporator, whilst the initial humidity has also to be established. These parameters are set during the gassing cycle development procedure, which is currently applied universally to new isolator systems. The parameters are monitored during the cycle, but they take no active part in the control of the cycle, the values being simply recorded. Given this scenario, most users opt for setting parameters that give the biggest "hit" of hydrogen peroxide vapour, with high ppm levels. Such users are keen to establish log 6 reduction in the shortest possible time, taking little account of any potential for developing a more optimised cycle. Whilst this approach has perhaps satisfied the regulators so far, the lack of sophistication is becoming more obvious.

To assist readers, and for clarity, the four phases of the hydrogen peroxide vapour bio-decontamination cycle as well as the recommended terminology are described in the box.

Active cycle control

The active control of the VPHP cycle parameters, on a feedback loop system, offers major advantages. Unfortunately, this has not been possible until recently because the available sensors needed to deliver control feedback have had too greater time constant, and have relatively poor repeatability. However, the advent of the Vaisala combined vaporized hydrogen peroxide and humidity sensor has opened up new horizons. This instrument can provide a real-time signal for both the ppm level of vaporized hydrogen peroxide, and a measure of what Vaisala term "Relative Saturation".[1,2] As described in this paper, at 100% Relative Saturation, (RS) both hydrogen peroxide and water vapour condense at the same time, forming the frank, visible condensation that should generally be avoided in VPHP bio-decontamination cycles.[3,4]

Using this new instrument, it is possible to provide active control through the gassing cycle, of both the ppm level of hydrogen peroxide, and the RS. In this way, the RS can be held just short of frank condensation, while the

The phases of the hydrogen peroxide vapour bio-decontamination cycle

Whichever type of vapour generator is used, the hydrogen peroxide vapour bio-decontamination cycle is generally considered to consist of four distinct phases. These phases have been variously named by the manufacturers, but unfortunately some are confusing and, arguably, inaccurate. The main issue lies with the use of the word "conditioning" for the second phase of the cycle. The word "conditioning", in the context of air handling means primarily cooling, but also dehumidification or re-humidification. Therefore, using that word to describe the gas build-up phase, after the actual dehumidification phase, is bound to cause confusion.

The four phases of the VPHP bio-decontamination cycle are best described as follows:

1. Dehumidification:
The humidity of the air in the complete system is reduced to a known level, below 50%. Note that the humidity is reduced, and not taken down to near zero, which is not required for a valid cycle.

2. Gas build-Up:
The concentration of vapour in the system is increased to a known level. It is desirable to achieve the target level as quickly as possible

3. Dwell:
The concentration of vapour is held constant at the target level, for a period of time. That time is determined during gassing cycle development, and will generally be that which achieves a demonstrated log 6 reduction of the chosen BI, plus a chosen safety margin, e.g. 50%.

4. Aeration:
The concentration of vapour is bought down to the 8-hour OEL level of 1 ppm, or less. Again, most operators will seek to achieve a vapour concentration under 1 ppm as quickly as possible, in order to start process work. Note that following aeration, the ventilation of the aseptic chamber (e.g. an isolator) must be kept running to avoid vapour concentration rising once again, due to de-gassing of the various surfaces.

The word "sterilisation" should not be applied to the VPHP cycle which is a highly effective process when carried out correctly on clean surfaces, but cannot technically be considered as anything more than bio-decontamination.

ppm concentration is maintained at a level optimised during the gassing cycle development (GCD) exercise. This method automatically decreases the variability of conditions from batch to batch and leads to more stable ppm levels during repeated gassing cycles. The instrument can, of course, provide not only the cycle control, but also a readout of the ppm level and the RS to deliver positive documentary confirmation of each cycle.

Gassing cycle optimisation

The target of the majority of gassing cycle developments is generally the demonstration of log 6 reduction in the shortest possible time, as mentioned above. The intuitive approach to this has generally led to high ppm levels of peroxide during the biodecontamination phase of the cycle, sometimes even with values in excess of 1,000 ppm. However, users have reported relatively fast log 6 reduction with much lower concentrations, down into the low hundreds. These apparently disparate results derive from the nature of the VPHP process, specifically the micro-condensation which has been extensively described elsewhere.[3, 4]

The use of lower hydrogen peroxide concentrations is attractive for a number of reasons. It may for instance offer:

- Reduced aeration times
- Reduced gas build-up time
- Reduced overall cycle time
- Fewer issues with post-cycle degassing
- Less peroxide used
- Lower risk of damage to delicate equipment
- Lower risk to personnel

It would therefore seem reasonable to suggest that gassing cycles should not simply seek log 6 reduction, but should also seek to optimise the cycle to a relatively low ppm concentration. With the use of the real-time data that the Vaisala instrument can provide, this exercise is potentially fairly easy to carry out.

Proposal for research – gassing cycle optimisation

Neither of the authors has the facility to carry out the research and development work needed to demonstrate the methodology for cycle optimisation. Such work would require a small isolator, a VPHP generator, and a Vaisala peroxide instrument, together with microbiological capability to incubate BIs. Only a few BI sites would be needed in the isolator, and multiple cycles could be run back-to-back with for example, varied gas build-up times. The use of enzyme indicators would speed the process but would add to the costs. This exercise would be well suited to a university higher degree course.

Proposal for research – gassing cycle active control

Again, neither of the authors has the facilities to develop a VPHP generator with active control, but this should be well within the capability of any gas generator manufacturer. In essence, it is suggested that the ppm level feedback from the Vaisala instrument would actively drive the delivery of hydrogen peroxide solution to the vaporiser. The ppm level during the gas dwell phase would thus be maintained at a value set by the operator, within limits that would become apparent as the work proceeds.

At the same time, feedback of the RS from the Vaisala instrument might be linked to the air / gas delivery rate, in order to hold the RS just short of frank condensation. There is an interaction between the ppm level, the RS and the air / gas circulation rate that would need to be explored.

We understand that the Finnish company Cleamix has already incorporated this technology into a new range of hydrogen peroxide vapour generators. They use the measured ppm to maintain the desired ppm level, and the RS to control the humidity to avoid frank condensation.

Conclusion

The Vaisala peroxide instrument offers the potential to control VPHP bio-decontamination systems actively, giving more precise cycle control than the current practice of parametric methods. It also produces a real-time record of the cycle, ideal for documentary support, and validation.

The instrument could also make the optimisation of VPHP cycles a regular feature, with faster cycle times, reduced aeration times and fewer de-gassing issues.

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Tim Coles, BSc (Hons), M.Phil., Technical Director, Pharminox Isolation Ltd., has worked in the field of isolator technology for over twenty years. He was a founding member of the UK Pharmaceutical Isolator Working Party that produced *Pharmaceutical Isolators*, Pharmaceutical Press, 2004, and more recently of the PDA committee that produced Technical Report No 51: *Biological Indicators for Gas and Vapour Phase Decontamination Processes* [for the validation of isolator sanitisation]. His book Isolation Technology – a Practical Guide, CRC Press Inc. 2004, is now in its second edition.

Sanna Lehtinen is a Product Manager at Vaisala. She has worked as an electronics designer and with life science product management in leading international high tech companies for 20 years. At Vaisala, Sanna ensures product quality and road mapping, gathers industry insight, develops leading products for demanding customer needs and produces relevant customer-facing material. Sanna holds an MSc in Biomedical Engineering from Tampere University of Technology and an MSc in Economics from Helsinki School of Economics.

GMP-compliant environmental monitoring systems in stem cell and tissue laboratories: Seven frequently asked questions

Hasim Solmaz

Abstract

New innovations in the field of medical technology bring with them special demands. Stem cell based treatments are undoubtedly amongst the most successful of the new treatments developed in recent years. The complex structure of stem cells demands specifically controlled environments for research, production, storage and delivery. As with traditional pharmaceutical products, many different items of laboratory equipment are involved as well as cleanrooms. All of these need monitoring in terms of regulatory compliance, efficiency and quality. In this article, the author shares with you the questions he often encounters in his native country Turkey – together with his answers.

"In cases where areas are not manned or the operator not present, the alarm and warning parameters for protecting the samples and products can be transmitted to the persons responsible by e-mail, SMS, voice message and other remote warning methods."

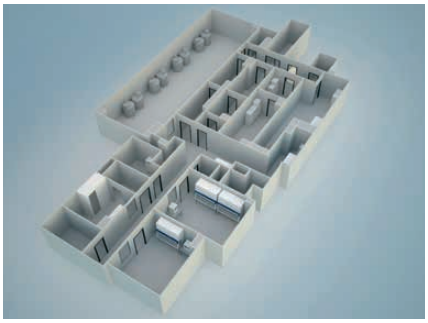


Figure 1: A schematic layout of a typical stem cell laboratory

Seven typical questions answered

Q1. What equipment should be monitored in stem cell laboratories and what are the monitoring parameters?

A: All equipment directly involved in the work-flow of the study, in which live cells are processed, must be monitored. In addition, all ambient conditions, starting from the differential pressure of adjacent rooms of the GMP Grade B cleanrooms at the first stage of the process, and including temperature and relative humidity, must be monitored as must the particle level in the GMP Grade A biosafety cabinets (BSCs) and the unidirectional airflow (UDAF) cabinets in which the study is done and the cells are directly open to the atmosphere.

Table 1 lists the equipment included in monitoring and the parameters monitored in a typical stem cell laboratory as shown in Figure 1.

Here are a few points to be noted;

- UDAF cabinets for testing and/or control, which are not directly

Table 1 - Equipment included in monitoring and monitored parameters

	Temperature	Relative Humidity	Differential Pressure	Particles	Oxygen	Carbon Dioxide
GMP Grade C/B Production Air Lock (Airlock)	√	√	√			
GMP Grade B Production Corridor	√	√	√			
GMP Grade B Production room	√	√	√	√		
BSC (Grade A)				√		
UDAF Cabinet (Grade A)				√		
Incubator	√				√	√
Drying Oven	√					
Refrigerator	√					
Deep Freeze	√					
Ultra Deep Freeze	√					
Cryogenic Tank	√					
Quarantine room	√	√	√			
Quality Control room	√	√				

involved in production, do not need to be included in the online monitoring system. The aim of a GMP-compliant monitoring system is to directly monitor the product and the environments in direct contact with the product. The same also applies to other laboratory equipment.

- By taking into consideration the specific circumstances of the site, a risk assessment should be carried out on-site. For example, a Grade B corridor that is used actively and in which the sample is processed/ packaged or tested, should be treated as an active room and particle monitoring should be performed in the room. Similarly, differential pressure monitoring across all actively used sterile rooms of the cleanroom will help reduce the risk.
- Multiple sensors can be used in sensor placement taking into account room/device sizes and sections used independently and for different purposes.
- In cleanrooms, the operator room and areas with cryogenic tanks should contain alarm towers to warn operators directly with auditory and visual alerts. These alarm towers must be coded to indicate normal status, alarm status and action status in green, yellow and red respectively.
- In cases where areas are not manned or the operator not present, the alarm and warning parameters for protecting the samples and products can be transmitted to the persons responsible by e-mail, SMS, voice message and other remote warning methods.

Q2. Are there any standards and regulations that apply to these environmental monitoring systems?
A: Stem cell laboratories have areas classified as A, B, C and D in EU GMP Annex 1.[1] These areas should be monitored in accordance with the requirments of the section on viable and non-viable environment and process monitoring in Annex 1. In addition, a risk-based approach for computerized monitoring systems including validation is comprehensively covered in GAMP5 (Good Automated Manufacturing Practice Vol.5) document published by the International Pharmaceutical Engineering Association (ISPE). ICHQ9 "Quality Risk Management" document, published by International Conference on Harmonization (ICH), is also particularly helpful in the pre- and post-installation risk assessments.

Q3. We have a building monitoring system, do we still need a seperate environmental monitoring system?
A: Perhaps the most common question regarding continuous monitoring systems in stem cell laboratories is whether the data collected by a Building Management System/Building Automation System (BMS) can be used as Environmental Monitoring System data in terms of quality. First of all, a BMS system is an automatic system that controls the heating, cooling and air conditioning (HVAC) system and collects data accordingly. The purpose of the environmental monitoring system is to ensure quality. The comparison in Table 2 shows that the BMS and the environmental monitoring system are clearly dissimilar.

Q4. The equipment we use measures and controls all the necessary parameters in that equipment. Is this infrastructure sufficient to monitor the system?
A: Just like building automation systems, equipment such as drying ovens, incubators, refrigerators, deep freeze and cryogenic tanks used in the laboratory can provide data from their own internal interfaces and can transfer these data to a central software system by means of these interfaces if desired. However, GMP-compliant environmental monitoring systems provide a second level of security since they also monitor potential sensor malfunctions as well as the data that controls the devices. Similarly, in the event of a failure in the GMP-compliant environmental monitoring system, the internal sensors of the devices help to guard against possible errors and losses.

Table 2 - Differences between building automation systems and environmental monitoring system

	Building Automation System (BMS)	Environmental Monitoring System
Purpose	The main purpose is to control the building air-conditioning system, fire detection system and security system.	To detect any possible off-limit condition and to warn the operator in the production process.
Sensor Position	For environmental data, the sensor points are air returns, culverts and service areas.	Sensor points in the field are selected by a risk-based approach, considering the worst-case scenario and with thermal mapping where necessary.
Warning and Control	Data is collected for purposes of establishing control parameters for HVAC and other systems and not for communication with operators.	Any possible warnings in the field are transmitted directly to the operators by means of alarm towers with audible, visual warnings. The system has no function to control. The goal is to collect and interpret the data accurately and to identify possible deviations.
Validation	Not necessary. Data accuracy and continuity are not top priority.	It is essential that the system is validated, and all errors, failures and data loss scenarios are examined in Design Qualification and tested in IQ and OQ phases.
Calibration	Sensors are generally not subjected to regular calibration as long as they are functioning properly.	The sensors are calibrated at least once every 6 to 12 months.

Q5. We use a datalogger to collect all critical data. Is it enough?
A: Data collectors can play a key role in determining trends and logging alarm incidents. However, they cannot replace GMP-compliant environmental monitoring systems. In case of a possible alarm state, unless the data on the data collector is transferred to the computer in real time, operators are only notified of this alarm condition after the intervention time period has expired. Usually we use data collection devices for heat mapping, worst case scenario and trend tracking. With GMP-compliant environmental monitoring systems, the aim is to inform the operator in the fastest and most effective way possible in case of a potential state of alarm.

Q6. Can data from building automation system (BMS) sensors differ from the GMP-compliant environmental monitoring system data?
A: In BMS systems, the sensor placement is designed to collect enough data to enable the HVAC system to function most efficiently. Thus, for example, the temperature data is taken from the return air and/or the fresh air ducts for the room. In this case, with a risk-based approach, values measured at the selected point in the room may differ from the values at the selected point in BMS. If the sensitivity, calibration status and hysteresis of the sensors are taken into consideration, the values may not be exactly the same. Since GMP-compliant monitoring systems are validated in accordance with GAMP5, each sensor is tested with a reference sensor at the time of operational qualification and the accuracy of the data is confirmed. Therefore, it should not be expected that the data from BMS and from environmental monitoring systems are necessarily the same.

Q7. Should particle monitoring systems utilise 1 cubic meter air sampling?
A: We often encounter this question not only in stem cell laboratories, but also in pharmaceutical manufacturing facilities. First of all, EU GMP Annex 1 provides guidance on both cleanroom classification and cleanroom monitoring. Clauses 4 to 7 of this document cover "Cleanroom and clean air device classification" and Table 3 shows the classification table given in this section;

Sample volumes used for monitoring purposes using automated systems are generally a function of the sampling rate of the system used. The sample volume does not have to be the same as the one used for the official classification of clean rooms and clean air devices.

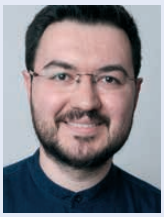
In clause 5 of EU GMP Annex 1, it is clearly stated that a minimum of 1m^3 of air should be sampled for Grade A for qualification studies carried out in cleanrooms. However, this is different in the case of continuous monitoring. Continuous monitoring is carried out under the conditions set out in clauses 8 to 15 of EU GMP Annex 1. Here, in clause 5 it is stated: *" ...Grade A areas should be monitored at any sample volume and measurement frequency which can trigger all kinds of interventions, transient events and all kinds of system disturbances by triggering off-limit alarms."*. Clause 12 states: *"Sample volumes used for monitoring purposes using automated systems are generally a function of the sampling rate of the system used. The sample volume does not have to be the same as the one used for the official classification of cleanrooms and clean air devices."* For this reason, suitable volume samples should be taken at frequent regular intervals, typically every minute. These should be compared with the alarm limits and the operator must be warned where the alarm limits are exceeded.

References

1. EU GMP Annex 1 2008 Eudralex Volume 4, EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use, Annex 1 Manufacture of Sterile Medicinal Products (corrected version). European Commission 2008. This document is currently under revision.

Table 3 - Particle limits for each class in EU GMP Annex 1

	Permissible particle limit of 1m^3 of target particles of equal and larger diameter			
	At Rest		In Operation	
Grade	0.5 Micron	5.0 Micron	0.5 Micron	5.0 Micron
A	3,520	20	3,520	20
B	3,520	29	352,000	2,900
C	352,000	2,900	3,520,000	29,000
D	3,520,000	29,000	Not Defined	Not Defined



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Cleanroom known unknowns: 4. Airlocks

Andrew Watson

Abstract

This article explores the known unknowns associated with airlocks and change-rooms. Design guidance, which is taken literally all too often, can lead to over-engineering and unnecessary complexity. This article looks at the fundamentals of airlock location and design and how systems of airlocks can help or hinder the operation of a cleanroom. We know that we need airlocks, but how many do we really need? The simple answer is "less than you might think", but as usual, the reality is a lot more complex.

Airlocks and change-rooms

Working as a cleanroom designer, assessor and remediator, you often get asked questions that in your own mind have a black or white answer. However, in reality your response must navigate tradition, superstition and prejudice, be drawn from vague guidelines, previous experience and cultural knowledge, consider costs, operator convenience and health and safety and all the while trying to sound sensible. Answering a simple question about the use of a HEPA filter will have several different answers, depending on where I am in the world.

Generally, the shady grey nature of my responses stems from the general ignorance of the scientific principles of how a cleanroom works. Now I make this statement not just to denigrate myself, or, heaven forbid, my clients. Rather, to denigrate the industry as a whole. I have characterised this before as a chronic lack of curiosity, and it manifests itself in the form of over-designed and over-complicated facilities that are hard to work in, cost a fortune to run and are full of bells and whistles that can only be kindly described as redundant.

I will save my scorn for much of the hocus pocus devices that fill my inbox and crowd exhibition floors for another time. Instead, I'm going to look at something more fundamental.

In this fourth instalment of the Known Unknown series I am going to tackle airlocks and change-rooms. These have a fundamental purpose in cleanroom design, yet so often they are poorly applied to a layout, badly designed and can, at worst, make a cleanroom almost unusable.

"Often, we take a progressive approach, with a discrete gowning or decontamination step for every move into a more critical area. This approach applies more control to the activity, but also more complexity, more movement and potentially more opportunities for mistakes or short-cuts by staff."

Basically, airlocks provide a specific 'break' between rooms of different cleanliness classifications. There are other reasons too; gowning is a messy business and de-gowning even messier: the airlock contains these activities and should prevent contamination reaching the cleaner room. Further measures can include separate personnel and material airlocks, separate gowning and de-gowning airlocks and sometimes even clean 'buffer' rooms in which you literally do nothing other than pause before you enter a critical area. Often, we take a progressive approach, with a discrete gowning or decontamination step for every move into a more critical area. This approach applies more control to the activity, but also more complexity, more movement and potentially more opportunities for mistakes or short-cuts by staff.

In general, there are a few basic guidelines, rules of thumb or 'understandings' that are applied to airlock application in a facility layout:

a. You need an airlock for each ISO step up and ISO step down. If you are going to from outside to an ISO 6 cleanroom, you will need to go through an unclassified/ISO 8 airlock, then an ISO 8/7 airlock and then an ISO 7/6 airlock on the way. The PIC/s guidelines provides a nice shortcut to this by coming up with the Grade A, B, C and D, but reinforces the iterative approach, if present thinking on EU GMP Annex 1 is anything to go by.[1]

b. Air from a higher classification should never mix with a lower classification. For example, never let ISO 8 air into an ISO 7 room.

c. The much-debated statement in the current Annex 1:[2] "The final stage of the changing room should, in the at-rest state, be the same grade as area into which it leads" leads to the addition of buffer rooms and timing devices on door interlocks that slow movement into cleanrooms even further.

These three items are not necessarily based on science or common sense and are not even routinely followed. However, in the absence of wiser heads they can lead to facilities of labyrinthic complexity. Throw in some left field elements such as infectious or hazardous materials, incompatible products and multistage processes and you frequently find that you cannot design a facility while complying with these three requirements.

So, perhaps we can bring out the science and see if we can find a better way. Some key (and somewhat obvious) points:

- It is well established, not least by articles in this journal that the particle concentration at a specific point and time in a cleanroom is a function of the particles being introduced and the dilution by a certain volume of clean air.
- If the air is supplied through a HEPA filter it is the same level of cleanliness, whether it is introduced into an ISO 8 or ISO 5 room.
- A person in a specific gown is going to shed the same number of particles regardless of the classification of the room they are in.

- In terms of peaks of contamination and residence time in operation, consider the following:
  - Production rooms – if closed processes, moderate peaks, high residence time
  - Gowning airlocks – high peaks, low residence time
  - De-gowning airlocks – very high peaks, very low residence time
  - Corridors – low peaks, very low residence time
  - Buffer rooms – very low peaks, very low residence times
- Gowning airlocks only serve a purpose if you are actually doing some gowning. If you are going through three airlocks to get to your Grade B cleanroom, and only performing some gowning in the first and third, then what is the purpose of the second? The number of particles you are shedding when you leave the first airlock will be the same as when you arrive in the third.
- Attempting to put on a sterile gown while or just after someone else is de-gowning or has just done so is probably a bad idea. A separate de-gowning room should be considered. However, if your cleanroom works on a single shift, this is rarely going to happen, so a single airlock should suffice.
- Corridors are in essence buffer rooms. From a contamination control perspective, they serve the same purpose. A buffer room followed by a corridor is probably redundant.
- The use of 'bubbles' (higher pressure airlocks than the rooms they connect) or 'sinks' (lower pressure airlocks than the rooms they connect) are useful for controlling cross-contamination and contamination of unprotected areas. They are also useful for preventing those end-destination cleanrooms where the cascade of pressures can total over 100Pa.
- 'Bubble' or 'sink' airlocks challenge this traditional ever-increasing pressure as you move from dirty to cleaner rooms. There may be a small amount of leakage of air into or out of these airlocks in the wrong direction but the amount of air is usually small and you can generally make sure that any contamination will not be able to reach a critical zone by the judicious location of low level returns.
- The peak rate of contamination in a gowning room is probably the highest rate anywhere in the cleanroom suite. Therefore it follows that air supply rates should be the highest in the facility. Those designers that still use the "room classification dictates the air change rate" mantra never seem to take this into account.

In spite of this, there are still some unknowns that lead to design stand-offs:

- How many particles follow recently gowned staff into a cleanroom?
- How many are generally deposited onto their gown?
- How much does either actually matter? (I'd suggest that the latter is much more important than the former).
- Does a two minute pause after gowning in an airlock or a buffer room actually have an effect on the contamination that is taken into the cleanroom? (I'd say yes for airborne, but not necessarily for deposited contamination.
- Why would anyone think that a progressive cascade of de-gowning airlocks in the same manner as gowning airlocks is actually necessary?
- At what point does an overly complicated entry or exit system to a cleanroom become counter-productive? Compliance fatigue leads to short-cuts and rebellion. Multiple rooms reduce staff visibility and make supervision more difficult.

In many cases the addition of an additional airlock or buffer room is justified as it is the only way to get a design over the line. It removes twenty years' worth of future difficult questions and justifications. However, it might make it easier for the designer and the manager to justify, but it's the staff that have to live with it. The quantification of what a client, or an inspector or the staff will ultimately live with is possibly the greatest known unknown we face.

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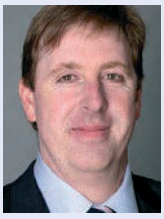

Andrew Watson is a Director of CBE, Centre for Biopharmaceutical Excellence, Australia. He is a Bachelor of Engineering (Chemical and has 25 years' experience in the design, construction, commissioning/validation and operation of a wide range high tech facilities, including pharmaceutical manufacturing, 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).andrew.watson@cbe-ap.com.au

Coronavirus pandemic shortages and the risks of using ineffective hand sanitisers in cleanrooms

By Tim Sandle

Abstract

Effective hand sanitisation using a alcohol-based sanitiser is an established part of cleanroom entry procedures. The coronavirus pandemic has led to supply shortages of hand sanitisers suitable for cleanroom use. Globally, regulators have relaxed some of the requirements for sanitiser manufacturers. This, coupled with subpar products entering the supply chain, could lead to inappropriate products reaching healthcare manufacturers. Included with products of concern are sanitisers containing methanol, as these are both microbiologically ineffective and highly-toxic. The risks are considered together with some best practice advice for purchasers of cleanroom consumables.

Introduction

Hand sanitisation (or disinfection) is an important pre-requisite for entering a cleanroom changing room. Depending on the facility layout, more than one hand sanitisation step may be required. This practice ensures that microbial contamination on hands is reduced. Hand sanitisation is different to glove sanitisation in that the disinfectant comes into contact with skin and therefore the product needs to contain moisturisers and emollients designed to avoid excessive drying and to minimise the risk of allergic dermatitis developing.

This hand sanitisation step has taken on additional importance during the coronavirus pandemic, in that effective hand sanitisation is one of the recommended contamination control measures for reducing viral transmission. A global shortage of suitable products due to the coronavirus pandemic[1] has led to new entrants coming onto the market, a process fuelled by regulators like the FDA waiving standards in order to increase supply. In Europe, there has been no pan-national reduction in standards (products must continue to meet the Biocidal Products Regulation (BPR) No. 528/2012).[2] However, individual member states were granted the ability to implement Article 55 of the BPR which allows for a temporary relaxation of the BPR regulations for up to 180 days initially, followed by up to a further 550 days if needed for a specific substance.[3] Furthermore, the shortage within Europe has seen imports rise from outside of the EU. Hence, managers of cleanrooms in the pharmaceuticals and healthcare sectors need to be cognizant to the risk of substandard and dangerous products entering the supply chain.

Importance of hand sanitisation and cleanroom entry procedures

In humans it is believed that approximately 80% of all microorganisms are transferred, from human-to-human or from object-to-object, by our hands.[4] This means that for cleanroom entry, hand sanitisation or hand washing stands as an important first line of defence against transfer of bacterial contamination. Training plays a fundamental part in any contamination control exercise. The correct washing technique, type of sanitisation or antiseptic agent to be used, frequency of hand sanitisation and more importantly the consequences of not following the basic principles are key in ensuring the safety of both operators / technicians and end-users of the product. The premise of effective application assumes that the agent is suitable and contains a sufficient level of water. Pure alcohols have limited effectiveness on the skin surface as they quickly evaporate which results in low contact times for penetration through the cell membrane of the microorganism. Typically a mixture of 60% or 70% alcohol to 30% purified water is used. The addition of water helps to facilitate the diffusion through the membrane of the bacterial cell or to inactivate viral genetic material. This formulation also improves the skin contact time by slowing down evaporation.

With hand sanitisers, in both Europe and the US, authorisation must be obtained for products that have a biocidal function designed to reduce microbial numbers and protect humans against harmful microorganisms through the action of the active substance they contains. The biocidal function is the consequence of the active ingredients, which will vary for different disinfectants. According to the World Health Organisation, the specification for an effective hand sanitiser is:[5]

- Alcohol (ethanol) (80% volume/volume) in an aqueous solution; or isopropyl alcohol (75% v/v) in an aqueous solution;
- Glycerol (1.45% v/v);
- Hydrogen peroxide (0.125% v/v); and
- Sterile distilled water or boiled cold water.

Risks with poor quality hand sanitisers

One consequence of the global pandemic has been a shortage of disinfectant products, including hand sanitisers. To meet the global demand, and to meet the void created by established disinfectant companies being unable to meet demand, other companies have entered the production space. This is either by producing alcohol to be used in sanitisers and then selling this to disinfectant manufacturers (as some brewing companies have done, as well as the owners of the Louis Vuitton, Givenchy, Tiffany, and Christian Dior lines)[6] or by creating start-up businesses to produce hand hygiene products. A concern is that many of these companies are not producing safe or efficacious products.

Relaxation of global regulations

One reason why so many substandard products have entered the market is because the FDA has waived its own standard for the supply of hand sanitisers in order to accelerate the supply. The FDA's temporary enforcement discretion policy is outlined in its guidance: *"Guidance for Industry: Temporary Policy for Preparation of Certain Alcohol-Based Hand Sanitizer Products During the Public Health*

Emergency (COVID-19).[7]" This document was issued on the 27th March 2020 and then updated on 15th April, 1st June and most recently on 7th August of the same year.

Exemptions included within the temporary policy are:[8]

- Formulation,
- Labelling,
- Adverse event reporting,
- Registration and listing.

Products designed for use in surgery, such as for skin disinfection prior to a procedure like catheterization, were not included in the temporary guidance (i.e. no modification is permitted). These are products where the active ingredients are chlorhexidine or quaternary ammonium compounds. For all products, the guidance permitted the production of aqueous solutions only (in other words, no aerosol, gel or foam presentations).[9]

While, arguably, standards have been stronger in Europe, European health and pharmaceutical companies will nevertheless draw on international supply chains. Globally, due, to these factors, the risk is that substandard products will enter the healthcare or pharmaceutical supply chain.

Methanol contamination of hand sanitisers

The FDA guidance did maintain the importance of only using products where the active ingredients are either isopropyl alcohol or ethyl alcohol (ethanol). For safety reasons these alcohols need to be denatured. Furthermore, the only permissible inactive ingredients are glycerine, hydrogen, peroxide and purified water (other ingredients, either active or inactive, such as might be added to alter the aroma, cannot be introduced since for safety reasons the product must smell like alcohol to discourage accidental ingestion). The guidance also stated that no product should be marketed with inflated superiority claims or labelling which was in any such way false. This includes any claim that a disinfectant can inactivate the specific coronavirus causing the spate of COVID-19 symptoms, because no specific disinfectant test standard has been developed for SARS-CoV-2.[10]

During August 2020 the U.S. Food and Drug Administration (FDA) had issued warnings about certain hand sanitiser products. Generally the warnings fell into two groups: either because of methyl alcohol (methanol) contamination (an alcohol that is toxic to human health) or because of sub-potent levels of alcohol (70% and above is regarded as effective at killing skin bacteria and 61% and above is considered effective at killing the SARS-CoV-2 virus).

Unscrupulous or ignorant manufacturers are using methanol in the hand sanitiser production process.

Other warnings were regarding the use of methanol which is not very good at killing microorganisms, compared to isopropyl and ethyl alcohol (a fact established during the 1920s)[11] and toxicity concerns have been known of since at least the 1930s.[12] Unscrupulous or ignorant manufacturers are using methanol ('wood alcohol') in the hand sanitiser production process. Methanol's practical use is as an industrial solvent, not as a disinfectant. The FDA has described such adulterated products as dangerous and toxic to human health. Moreover, there has been some reports of consumers experiencing serious side effects from methanol poisoning as a result of skin damage (it is easily absorbed into the dermis) or more dangerously, by ingestion (unfortunately something that is not as uncommon as readers might expect).[13] The hazards of methanol ingestion include nausea, vomiting, headache, blurred vision, and seizures. In very serious cases, permanent blindness, coma, permanent damage to the nervous system and even death can occur. This happens as the liver digests alcohol using an enzyme called alcohol dehydrogenase. Whereas ethanol is broken down into acetate, which is essentially harmless in low quantities, methanol is broken down into formic acid which is toxic. Aside from methanol, other ineffective hand sanitisers have been found to have been produced using 1-propanol, which is different to isopropyl alcohol and classed as a harmful toxin.[14]

From the manufacturing perspective, some hand sanitiser products are 'over-the-counter' products and do not require prior approval. These include household soaps and gels. However, for the products to be marketed as biocides then the formulation of such products must conform to national or European regulations..

Under the temporary measures, the FDA has been forced to issue several alerts about substandard products entering the market. These are primarily products labelled as containing ethanol which are later shown by agency testing to be partial or wholly methanol containing sanitisers. To date, the FDA has issued warnings about over 100 hand sanitiser products.[15] Many of these products of concern have been subject to recalls or import bans. In the US, purchasers have a legal and welfare responsibility not to purchase products from the proscribed list, which is maintained by the FDA. In Europe, observing the list is an important measure for protecting employee safety. This proactive measure becomes more challenging when products are purchased through third-party suppliers. A compliant vendor should be conducting analytical testing on samples to confirm their suitability. All this applies especially when new vendors are being considered.

Cleanroom controls

In these more uncertain times, cleanroom managers should assess products for:

- The exact same product name.
- The exact name of the active substance(s), and ensure this is ethanol or isopropyl alcohol.
- The exact % content of the active substance(s).
- The relevant instructions for use.
- The type of formulation.
- Name and address of the manufacturer.
- Safety and sustainability notices.
- Disposal details.
- Poisons Information.

These details should also be verifiable against a certificate of conformance. In terms of assessing hand sanitiser efficacy, a bacterial test is established. This is European Standard EN 1500: 2013 (or the equivalent international standard in other territories).[16] This standard specifies a test

method that simulates practical conditions for establishing whether a hand sanitising agent reduces the release of transient flora according to the requirements when rubbed onto artificially contaminated hands of volunteers.

Summary

Hand sanitisation is necessary for all staff entering changing rooms leading to cleanrooms. Due to supply shortages, many procurement departments have turned to new suppliers and many of the suppliers active in the market do not have established track records. This situation means that sub-potent or products containing toxic methanol can enter the supply chain, leading either to the use of products that will not kill skin bacteria sufficiently or inactivate the coronavirus, or which pose a threat to human health. Given the current concerns associated with some hand sanitisers, pharmaceutical and healthcare cleanroom consumable purchasers should undertake a risk assessment with their chemistry colleagues to assess that products offered by new suppliers are both suitable and safe for use.

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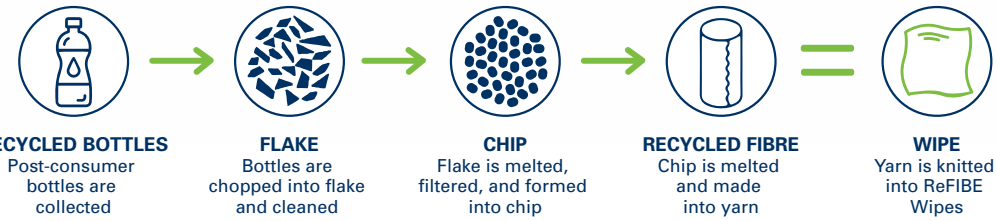
#cleangreen

From Waste to Wipe

Contec introduces a range of cleanroom wipes manufactured from recycled materials



Contec ReFIBE Wipes - Recycled 100% knitted polyester cleanroom wipes - providing a sustainability story in a single-use world.

Contec's range of ReFIBE cleanroom wipes provides a sustainable solution for critical environments without jeopardising quality or performance.

Each cleanroom wipe is constructed from 100% post-consumer recycled plastic bottles (35+ bottles per pack of wipes), saving waste from going into oceans or landfill. The bottles go through a rigorous cleaning process before being converted into polyester chip, which is then extruded and spun into yarn before being knitted into fabric. See more at **www.contecinc.com/refibe**

CONTEC® | WHATEVER IT TAKES™

ReFIBE™

Test results and methodology in validation

Tim Coles

Sir,

For the second time, we have recently been asked to review the validation of an isolator suite, for which the manufacturers have provided OQ protocols which split out the test results from the methodology. In the first instance, this caused frustrating delays because it was physically difficult to marry up the two parts of each test or check. The second and more recent instance is rather more worrying. Here the manufacturer not only separated the methodology from the results, but also refused to give access to the methodology except at their site, under full audit conditions. Worse still, under the current Covid 19 pandemic, no access to their site was allowed, rendering the methodology completely unavailable.

The manufacturer in question tells us that their isolators have been approved by the MHRA, and so by inference, the withholding of test methodology is deemed acceptable. This strikes us as contrary to the basic tenets of pharmaceutical (and other) validation. As far as we understand the principles of validation, each test or check should be structured thus:

- Name of test
- Purpose of test
- Method statement
- Criterion of acceptance
- Tables of results
- Pass/ fail statement
- Comments

We would absolutely question the validity of any test for which the methodology is withheld. By way of an example, imagine that you are about to set off on a motorway journey with your family. Wisely, you ask your mechanic to check the tyre pressures on your car. He assures you that all the tyres are at the correct pressure and you set off happily. However, you might not have put your family at risk had you known that the test methodology was to kick the tyres, and shrug the shoulders.

We would be most interested to hear confirmation from the MHRA , or indeed any other authority, that methodology can now be dropped from OQ protocols.

Yours sincerely

Tim Coles
Technical Director
Pharminox Isolation Limited

Mobile Energy Monitoring Units from EECO2 – remote, independent monitoring of plant and components

More and more companies are committed to working towards a Net Zero future. With HVAC typically accounting for 50-80% of energy usage in the pharmaceutical and high-tech sectors, and with systems being crucial for compliance, the ability to independently monitor and analyse energy usage and system status has never been more important.

EECO2's Mobile Energy Monitoring Units (MEMUs) allow not just energy consumption but also functions such as filter status in HVAC systems to be monitored from anywhere the world.

The MEMUs are simple to install – wireless plug and play in many cases, can be used across a number of applications from AHUs to lighting systems, and provide an immediate, accurate and independent record of the energy usage and filter status of those systems.

MEMUs can also be incorporated into a comprehensive site wide Monitoring & Targeting (M&T) scheme, to help drive continuous energy efficiency improvements.
Web: www.eeco2.com
Email: info@eeco2.com

Pharminox works on site through lockdown

As is probably the case for any company working in the healthcare sector, Pharminox Isolation Ltd has been operating steadily throughout the pandemic. Clients including the NHS and a vaccine company have issued us with documents indicating that we are required to travel for covid-related operations. Accommodation close to site was a problem in the early days of lockdown since hotels and restaurants were all closed, however we found that Airbnb were able to provide self-catering apartments. We have been required to work in locations which have subsequently emerged as covid hot-spots, but by taking the appropriate safety measures, the company remains in full health so far. Some sites offered limited PPE, but we have generally used our own masks and gloves. Visors did not seem to be required, or appropriate, at the sites visited up to now. Although all of our staff are in the at-risk group being over 60, we feel that we have a duty to maintain our services for the collective health of the nation and beyond.

www.pharminox-isolation.com

ECOLAB completes their low residue line-up

Ecolab's popular Klercide Low Residue Quat (KLRQ) range, a quaternary ammonium-based daily disinfectant for cleanrooms is now complemented with the addition of Klerwipe Low Residue Quat impregnated Mop Wipes.

This convenient new format provides increased consistency in use, broad spectrum efficacy and the low residue profile of Klercide Low Residue Quat in a wipe for large surface disinfection. Its easy-to-use, high grade 100% polyester – specially selected for quaternary ammonium compounds – is a fully ready-to-use option from the renowned experts in cleanroom cleaning and disinfection solutions.

Being sterile, Klercide Low Residue Quat Mop Wipes are ideal for use in high grade cleanrooms where the increasing regulatory demands found in the latest draft of Annex 1 for example, make residue management a priority for the pharmaceutical industry.

Available in cases of 10 by 15 wipes, the addition of the Mop Wipes to the range means Klercide Low Residue Quat is now offered in seven formats, including the ready-to-use 1L trigger spray (Incorporating the patented SteriShield Delivery System) and 5L ready-to-use solution, 5L concentrate, unit dose and metered dose concentrates plus pouch wipes.

More information about Klercide Low Residue Mop Wipes and Ecolab's low residue approach can be found at www.ecolablifesciences.com/offering/low-residue-program

www.ecolablifesciences.com

Cut-resistant glove liners for cleanroom environments from Ansell

In order to protect cleanroom personnel against cut hazards, Ansell have developed BioCleanTM S-BCRL glove liners. These are sterile cut-resistant liners designed to be worn between two standard cleanroom gloves. Woven with Dyneema® Diamond yarn, they offer EN 338 and ANSI A2 cut protection for researchers/ operators working with apparatus or equipment that poses a moderate cut risk, whilst maintaining aseptic protocol in a controlled environment.

The glove liners are both powder- and latex-free to prevent any latex allergies, as well as the chance of contamination that arises from powder. This is a significant advantage over other cut resistant liners that are often not up to cleanroom standards and are packaged in paper, which is itself high in particles. BioCleanTM-S-BCRL gloves are packaged in individual EasyTear polyethylene wallets for convenience and cleanliness.

By blending spandex with an ultrahigh molecular weight polyethylene, the BioCleanTM S-BCRL gloves are lightweight and comfortable, whilst still providing the same cut resistance as other, thicker, less comfortable types.

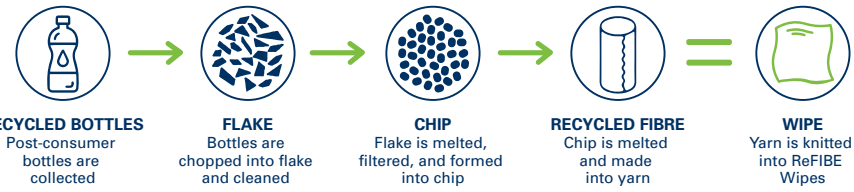
If you work in an aseptic cleanroom or controlled environment, and are regularly facing cutting and laceration risks, consider BioClean cut resistant liners.

For more information see Ansell cut-resistant liners.

From waste to wipe – Contec launches cleanroom wipes made from recycled materials

Sustainable consumable options that are appropriate for cleanrooms are difficult to find. Contec is excited to launch ReFIBE, the cleanroom industry's first sustainable polyester wipe that is made from recycled post-consumer plastic bottles.

There are multiple steps taken to make ReFIBE wipes. Recycled plastic bottles are collected, then chopped into flake and cleaned. The bottle flake is melted, filtered and formed into chips. These chips are melted and made into yarn. The yarn is then knitted into ReFIBE wipes.



ReFIBE are 100% standard weight polyester wipes and the particle and extractables data is very comparable to a traditional polyester wipe. ReFIBE wipes are laser-cut with heat-sealed edges

Each case of 9" x 9" wipes stops 840 plastic bottles going to landfill or ending up in the ocean.

For more information or to request a sample, go to www.contecinc.com/eu

Cherwell prepared media accessories help reduce risk in EM

Cherwell Laboratories has prepared media accessories for use within cleanroom environmental monitoring programmes, in response to customer demand. This is due to the increasing importance and need for continuous microbial monitoring in line with updated GMP regulations for the manufacture of sterile medicinal products.

Cherwell's range of accessories includes Settle Plate stands, reducing the risk of a spoilt sample. Holding one or two plates, the stand's configuration provides a place for the exposed plate and lid. The twin plate stand offers a solution where two types of agar are used.

Recently introduced, a tall version; where the plate stand is mounted on a rod, with a circular base for stability; can be placed in an optimal, non-intrusive location. Available at 800mm and 1,000mm heights, the stand can also be made to a customer specified height, or a twin plate version.

Also ensuring crucial agar plate protection and complementing the plate stands, Cherwell manufactures stainless-steel contact plate and petri dish carriers to aid safe handling and transportation and efficient use of incubator space.

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

Envair Technology announces acquisition of fume cupboard specialists TCS

Envair Technology has announced the acquisition of Lancashire based fume cupboard manufacturers Total Containment Solutions (TCS) in a deal worth £2 million.

The growth delivered by existing group companies ONFAB and Envair Limited has provided the platform for this next stage of the group's ambition to become the leading global clean air containment company. Envair Technology now offers an expanded product portfolio to clients in the healthcare, pharmaceutical and laboratory sectors.

Commenting on the investment, Gary Bagshaw, Envair Limited Managing Director, said: "It is just one year since Envair combined with ONFAB to create Envair Technology. In that time, we have continued to grow and thrive. This acquisition further widens our product offering and flexibility to respond to client needs."

Dave McCabe, TCS Managing Director, added: "Joining Envair Technology will bring significant benefits as we combine our expertise across the laboratory containment market, allowing us to serve customers even better."

From left to right: Gary Bagshaw and Andrew Ellison of Envair Technology Dave McCabe and Ian Bond of TCS

For more information visit:
www.envairtechnology.com
www.tcsltd.org.uk/

Envair isolators chosen for The Clatterbridge Cancer Centre – Liverpool

The Clatterbridge Cancer Centre NHS Foundation Trust is one of the UK's leading cancer centres. Its new Liverpool city centre building was opened in June 2020 and Envair was chosen to supply five negative pressure isolators and two rapid gassing vaporised hydrogen peroxide isolators for the new aseptic pharmacy.

This improved capacity has enabled two isolators to be dedicated to trials for advanced therapeutic medicinal products and gene therapy.

Jayne Kelly, Deputy Chief Pharmacist Technical Services, explained that the Trust chose Envair because of the company's reputation for engineering and service excellence. She also appreciated the proactive consultancy she received at the beginning of the project, when Envair's engineers advised on elements of the isolators, to which she and her team may not have given consideration, including the shape of the glove sleeves.

Jayne says that the team find the isolators especially easy to use, thanks to the Vari-Height work area, foot pedals and of course, those specially designed glove sleeves which have provided greater operator flexibility.

For further information please visit www.envair.co.uk/products/rigid-isolators/

The new normal is here from PMS

Companies want to protect their employees and keep pharmaceutical manufacturing running, while working effectively and getting product to market safely and quickly.

This presents a wide range of challenges that we did not face at the beginning of 2020. Fortunately, Particle Measuring Systems' PharmaIntegrity data management meets all the above requirements to enhance cleanroom management and particle counter data needs in the new normal. Working remotely you can access, manage, and report on particle counter data from any location in the world (including your home office). This includes getting 21CFR11 electronic signatures/approvals, managing inventory needs, getting trend reports to alert you to possible contamination issues before they occur, and reporting. You can securely access data from multiple connected facilities and run cohesive reports, trend analysis, identify stock that needs ordering, and more.

Learn more at www.pmeasuring.com/new-normal

Filter testing equipment from ATI during COVID-19

Air Techniques International (ATI) has been a global leader in the design and manufacture of specialized testing equipment for HEPA filters, media, filter cartridges, respirators, and protective masks since 1961.

Since the outbreak of COVID-19, ATI has seen an increase in interest and demand for cleanroom certification equipment (digital photometers and aerosol generators). Cleanrooms, like many businesses, have modified their operations to help protect employees from COVID-19 by increasing their supplies of PPE and hand sanitizers, installing protective screens, enforcing social distancing rules, and implementing alternating shifts.

While much is still unknown regarding COVID-19, the WHO's latest guidance does not rule out aerosol transmission of the virus. As such, Government bodies have suggested the close monitoring of air filtration systems, especially in medical-related facilities, to ensure proper airflow and purity of the air as added precautions.

ATI's 2i Digital Photometer and handheld iProbe are widely used by cleanroom certifiers to test HEPA filters for leaks. The 2i is portable, yet rugged, and is the ideal instrument for on-site filtration system integrity testing.

For more information about the 2i, visit https://www.atitest.com/products/2i-digital-aerosol-photometer/

Crowthorne for emergency recovery plans

Crowthorne's technical specialists have now created an upgraded version of their 'Biosafe' Emergency Recovery plan providing a more comprehensive service package to customers with Containment Level 3/Hazard Group 3 facilities. The new program offers 3 levels of cover, ranging from an annual sealability test to a full CL3/HG3 validation and fumigation service for complete compliance to HSE, HTM 03-01 and ACDP guidelines.

'Biosafe' can also be tailored to meet the specific needs of individual customers.

Please visit https://crowthornehitec.co.uk/contact/

Events

2020	Event	Location
September 29-30	Making Pharmaceuticals Ireland RESCHEDULED TO SEPTEMBER 2021	Dublin, Eire
October 5-8	ESTECH/EDUCON NOW VIRTUAL	Virtual
October 13-15	25th International Symposium on Contamination Control, ICCCS'20 RESCHEDULED TO OCTOBER 2022	Antalya, Turkey
October 26-27	Making Pharmaceuticals Exhibition and Conference RESCHEDULED TO JULY 2021	Coventry, UK
October 28-29	Cleanroom Technology Conference 2020	Birmingham, UK
October 28-29	Manufacturing Chemist Live 2020	Birmingham, UK
November 4-5	Lab Innovations	Birmingham, UK
November 17-19	International Congress A3P	Biarritz, France
November 18-19	Cleanzone	Frankfurt, Germany
November 24-25	Cleanroom Technology Conference 2020	Hyderabad, India
December 1-2	Cleanroom Technology Conference 2020	Singapore
December 16-18	EP and Clean Tech China	Shanghai, China
2021	**Event**	**Location**
May 3-6	ESTECH 2021	Baltimore, Maryland
May 25-27	Symposium & Exhibition 2020	Naantali Spa, Finland
June 14-18	Achema	Frankfurt, Germany
July 6-7	Making Pharmaceuticals Exhibition and Conference RESCHEDULED FROM OCTOBER 2020	Coventry, UK
September 28-29	Making Pharmaceuticals Ireland RESCHEDULED FROM APRIL 2020	Dublin, Eire
2022	**Event**	**Location**
October 11-13	25th International Symposium on Contamination Control, ICCCS'20 RESCHEDULED FROM OCTOBER 2020	Antalya, Turkey

Training courses

IEST (Institute of Environmental Sciences and Technology) www.iest.org		
2020	**Event**	**Location**
September 15	Cleanroom Cleaning and COVID-19	VIRTUAL
October 5	Basics of Cleanroom Design, HVAC System Design, and Engineering Fundamentals	During ESTECH/ EDUCON 2020, VIRTUAL
October 6	Cleanroom Basics: What is a Cleanroom and How Does it Work?	During ESTECH/ EDUCON 2020, VIRTUAL
October 7	Beyond Cleanroom Basics: Fundamental Information for Cleanroom Operations	During ESTECH/EDUCON 2020, VIRTUAL
October 8	Cleanroom Classification Testing and Monitoring	During ESTECH/ EDUCON 2020, VIRTUAL
November 10	Essential Cleanroom Standards ISO 14644-1 and ISO 14644-2: The Foundations of Contamination Control	VIRTUAL
November 11	New ISO 14644-3:2019 - Basic Information and Implementation	VIRTUAL
November 12	Universal Cleanroom Operations Guidelines with ISO 14644-5	VIRTUAL

CCN (Contamination Control Network) www.theccnetwork.org		
2020	**Event**	**Location**
November 10–12	CTCB-I Testing and certification course	Liphook, England

ICS (Irish Cleanroom Society) www.cleanrooms-ireland.ie		
2020	**Event**	**Location**
For a complete list of courses including CTCB-I courses, please see https://www.cleanrooms-ireland.ie/training/		

R3Nordic www.r3nordic.org Safety Ventilation www.safetyventilation.com		
2020	**Event**	**Location**
October 6-7	CTCB-I Testing & Certification, Associate Level	Gothenburg, Sweden
October 6-8	CTCB-I Testing & Certification, Professional Level	Gothenburg, Sweden
For courses run by R3Nordic see https://r3nordic.org/		

VCCN (Association of Contamination Control Netherlands)		
2020	**Event**	**Location**
For a complete list of courses including CTCB-I courses, please see http://www.vccn.nl/cursusaanbod		

TTD (Cleanroom Technologies Society of Turkey www.temizoda.org.tr		
2020	**Event**	**Location**
For courses run by TTD see https://www.temizoda.org.tr/en/trainings		

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

Life-lines

Quotations of Louis Pasteur

Messieurs, c'est les microbes qui auront le dernier mot.
(Gentlemen, it is the microbes who will have the last word).

The role of the infinitely small in nature is infinitely great.

A bottle of wine contains more philosophy than all the books in the world.

Wine is the most healthful and most hygienic of beverages.

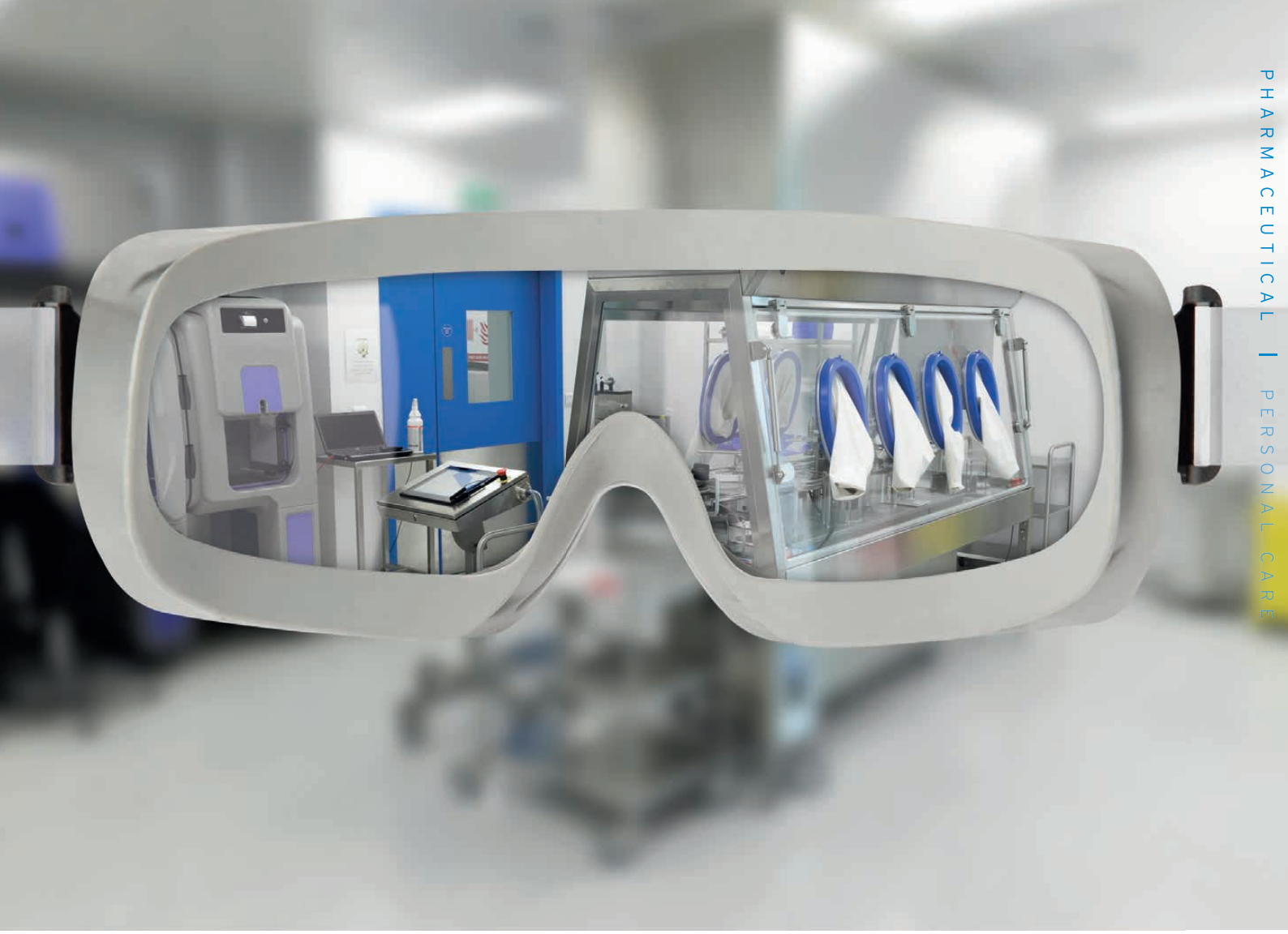
Science knows no country, because knowledge belongs to humanity, and is the torch which illuminates the world.

Dans les champs de l'observation le hasard ne favorise que les esprits prepares - Where observation is concerned, chance favours only the prepared mind.

Let me tell you the secret that has led me to my goal. My strength lies solely in my tenacity.

I am on the edge of mysteries and the veil is getting thinner and thinner.

I am utterly convinced that Science and Peace will triumph over Ignorance and War, that nations will eventually unite not to destroy but to edify, and that the future will belong to those who have done the most for the sake of suffering humanity.



PHARMACEUTICAL | PERSONAL CARE

A CLEARER VIEW OF **ANNEX 1**

Ecolab remains at the forefront of industry regulations, providing insight into the Annex 1 updates.

With the latest draft* making more exacting demands around cleaning and disinfection for pharmaceutical manufacturers, Ecolab can help your compliance with:

- A range of **product formats** which are sterile and ready-to-use as well as **Hydrogen Peroxide Vapor (H_2O_2) technology** that provides an aseptic processing environment
- **Validation** expertise through our Validex program
- **Service excellence** from our Technical Consultants to provide guidance around interpretation and implementation of the regulations

To help guide you through Annex 1, speak to your Ecolab account manager today, or visit our dedicated web page at

ecolablifesciences.com/annex1

ECOLAB LIFE SCIENCES
FOR LIFE SCIENCES. FOR LIFE

**Annex 1 of EudraLex Volume 4 - Good Manufacturing Practice (GMP) guidelines, draft 12 - February 2020*

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Everywhere It Matters.™