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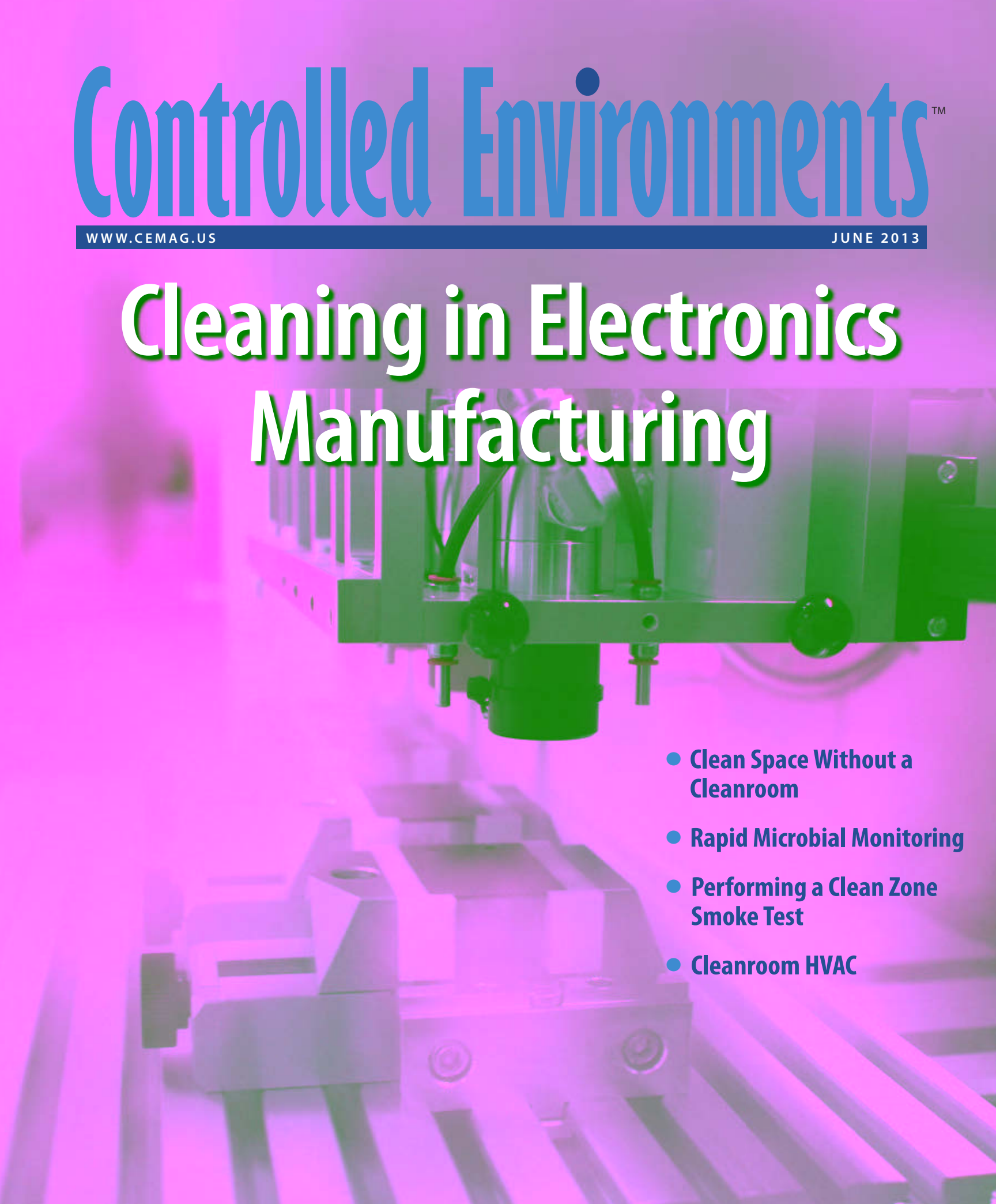
Cleaning in Electronics Manufacturing



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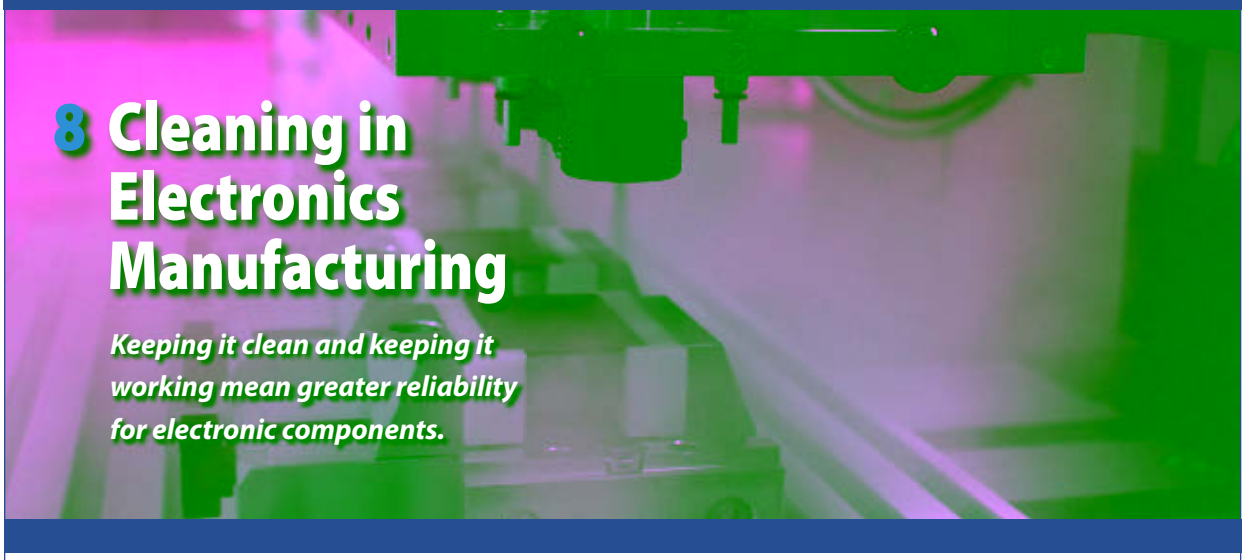
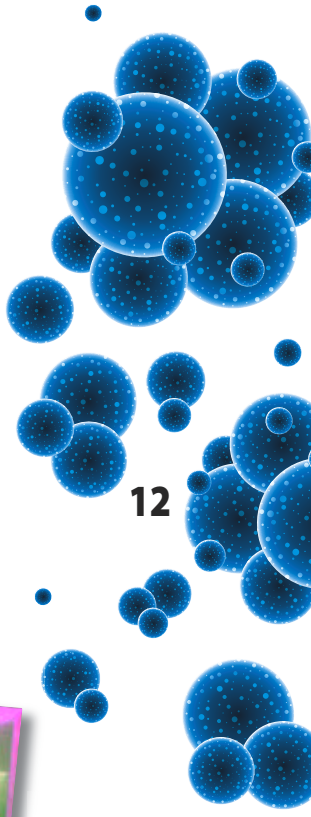
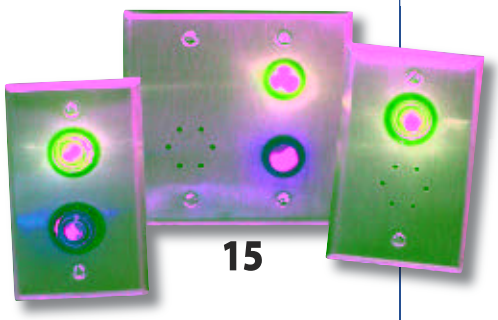


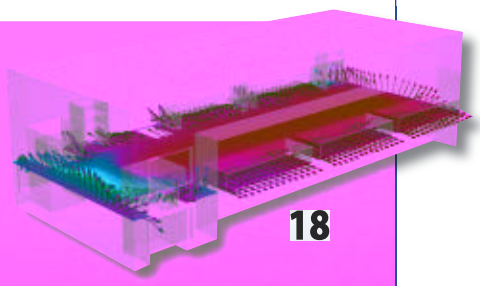
8 Cleaning in Electronics Manufacturing

Keeping it clean and keeping it working mean greater reliability for electronic components.

Cover image courtesy of ACP and Parts2Clean. See related article on p. 8







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Politics and BSL

Tim Studt
Editorial Director

The ultimate in controlled environments are biosafety level-4 (BSL-4) labs which are designed for work with severe to fatal diseases for which there are no known cures. There are about 52 BSL-4 (or P4 in Europe) labs either operating or under construction, with 15 of those in the U.S. One of those slated to begin lab construction in 2014 is the National Bio and Agro-Defense Facility (NBAF) planned to be built at Kansas State University in Manhattan, Kan. NBAF, which will have labs approved for BSL-2, -3, -3E, -3Ag, and -4 clearances, is the planned replacement for the aging Plum Island Animal Disease Center (PIADC, which operates labs up to level-3Ag) located since 1954 off the northeast coast of Long Island, N.Y.

PIADC was operationally transferred from the U.S. Dept. of Agriculture to the Dept. of Homeland Security (DHS) in 2002, following public calls for its closure for a variety of reasons. In 2005, the DHS announced that PIADC would be replaced with the NBAF. Pre-design awards were made in 2007 for the NBAF and the 574,000 gsf facility design was completed in July 2012. Several site-specific risk assessment studies for all biosafety levels for the NBAF were performed by the National Research Council (NRC) with the DHS stating that all recommendations identified in the risk assessment were incorporated into the final design.

While not the most expensive labs around (Class 100 GMP production facilities top that list at about $1,000/GSF primarily due to the massive air handling systems required), BSL-4 costs start at about $600/GSF and can include some substantial costs for exterior security.

Cost has become the latest concern in creating the NBAF. Initially estimated at about $650 million, the two laboratory buildings and four outbuildings at the Kansas site are now estimated to cost about twice the original budget —$1.255 billion. Funds for the NBAF were included in the recently submitted FY2014 budget proposal by President Obama, but they require another $202 million in matching funds be invested by the State of Kansas. Kansas has already invested an initial $105 million for the NBAF and another $35 million in research funding for transitioning the NBAF from the PIADC. The additional funds from Kansas are not assured as there is substantial opposition to spending more monies on a program already several years late in even starting construction.

The NRC study concerning risk assessment for the NBAF included forecasts that the facility would be expected to have a $3.5 billion economic impact on the state during the facility's first 20 years of use.

The study made clear the value of creating a new NBAF for protecting the nation against known threat agents along with emerging and unknown disease threats for both human and animal species. The capacity to support critical research and diagnostic programs for the study of foreign animal diseases and zoonotic diseases are directly linked to securing the health and wealth of the nation. But, as with too many government-sponsored and funded programs, the final costs and schedules for creating these types of facilities are not even close to the original estimates, which makes everyone wary of their ultimate cost and value.

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Cleaning in Electronics

Keeping it clean and keeping it working mean greater reliability for electronic components.

Doris Schulz
Schulz.Presse.Text.
Korntal, Germany

The ever-increasing demand for reliability, continuing miniaturization, and the growing number of faults in electronic components manufactured in no-clean processes all combine to put the focus back on cleaning in electronics manufacturing. The industry offers a variety of solutions to finding the optimal cleaning process.

The development of no-clean fluxes and soldering pastes has done much to turn attention away from the need to clean components in electronics manufacturing. For many components that are only used in non-critical atmospheric environments, this mostly poses no problem. However, where they are utilized in adverse environments (such as humid or fluctuating temperatures), the protective layer applied in the no-clean process can be gradually eroded, releasing ionizing substances that promote electro-migration and dendritic growth. This occurs chiefly in narrow spaces beneath components and between their connections or other contact surfaces.

Increased requirement for surface cleanliness

In addition, protective coatings (conformal coatings), progressive miniaturization, wire bonding, and the increased use high voltage components all call for a high level of surface cleanliness. A further aspect is the use of lead-free solders, containing a higher proportion of fluxes and more aggressive activators that can cause problems. Cleaning of electronic components also involves removing potentially hazardous impurities such as fluxes, residues of soldering agents and adhesives, and such contaminants as dust and residue from previous manufacturing stages.

Cleaning with water-based media is generally done in dipping systems with multiple cleaning and rinsing baths. ***(Photo: Amsonic)***

Choosing the right cleansing agent

A key factor in achieving economy and efficiency in the cleaning process is the selection of a suitable cleansing agent. Selection criteria include the nature and quantity of the impurities to be removed, and the subject material. Cleaning agents currently used in electronics manufacturing include solvents, water-based media containing alkaline surfactants, and water-based tenside-free cleaning agents.

The electronics industry mainly uses solvents containing non-halogenated hydrocarbons, modified alcohols, or hydrofluorethers (HFEs). HFEs were developed as an alternative to the previously preferred chlorofluorocarbons (CFCs), after CFC manufacture was stopped about 20 years ago due to their high potential for breaking down ozone. Non-inflammable HFEs have similar properties to CFCs, but pose no danger to ozone, do not persist in the atmosphere, and have low greenhouse gas potential. At the same time, they offer physical properties that are in demand for the cleaning of electronics, such as relatively high density, low viscosity, and low surface tension. These solvents are used in monosolvent, cosolvent, and bisolvent systems.

A monosolvent system usually uses a pure HFE or an azeotrope—a mixture of two or more components that vaporizes without changing its chemical composition. It is used to remove slight impurities such as light oils, halogen compounds, residue of easy clean solvent, particles, and dust.

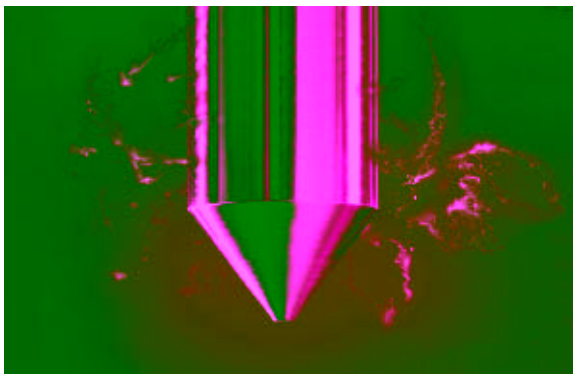
The cosolvent system consists of an HFE combined with a low-volatility organic solvent as a solubility promoter. The solubility promoter removes impurities from the surface of the workpiece and the HFE rinses away the solvent and the impurities from the components. Cleaning with a cosolvent procedure is extremely versatile and also gives good results with the most stubborn impurities such as heavy oils, grease, waxes, NC-flux residues, adhesives, and hot-melt glues. Choice of a low-volatility organic solvent allows material compatibility to be tested.

Cosolvent and bisolvent systems differ mainly in that, for the cosolvent system, the solvent and the rinsing agent are mixed together, while in the bisolvent process they are kept separate.

Manufacturing

Optimizing a process by adapting the plant technology

To ensure efficient and reproducible cleaning, it is essential to match the cleaning agent to the plant technology. That is why so many different cleaning systems are available, such as dipping plants with ultrasound or pressure



Ultrasound has a wide range of cleaning applications in the electronics and semiconductor industry. The cleansing sound waves are used in conjunction with solvents and water-based media. ***(Photo: Weber Ultrasonics)***

flooding and spray cleaning plants. Solvents are used today in totally enclosed cleaning units.

Ultrasound cleaning with solvents or water-based media offers a wide range of applications in electronics manufacturing. Another factor that influences the cleaning action, in addition to the cleansing agent, is the frequency of the electrical signals from the ultrasound generator, which converts the oscillating system to sound waves in the fluid bath. In general, the lower the electrical signal frequency, the greater the energy released by the sound waves. There are multi-frequency systems that permit acoustic irradiation of the goods to be cleaned at different frequencies; the optimum combination of cleansing agent and ultrasound frequency can be determined from cleaning tests, carried out by the equipment suppliers or the cleaning agent.

In selecting the type of cleaning equipment to use, key questions are: What throughput must be handled? What space is available in which to set up the equipment? How can the cleaning process be integrated into the manufacturing chain?

Dry alternatives with carbon dioxide

Cleaning with compressed carbon dioxide provides an extension to the wet-chemical process. The term "compressed carbon dioxide" indicates CO_2 that has been converted to liquid form (that is, into its supercritical phase) under pressure; in this form, it possesses excellent proper-

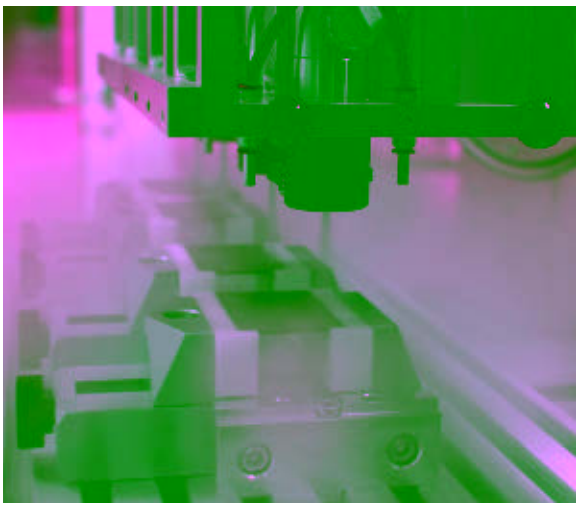
parts2clean international trade fair

parts2clean is the leading international trade fair for industrial parts and surface cleaning.

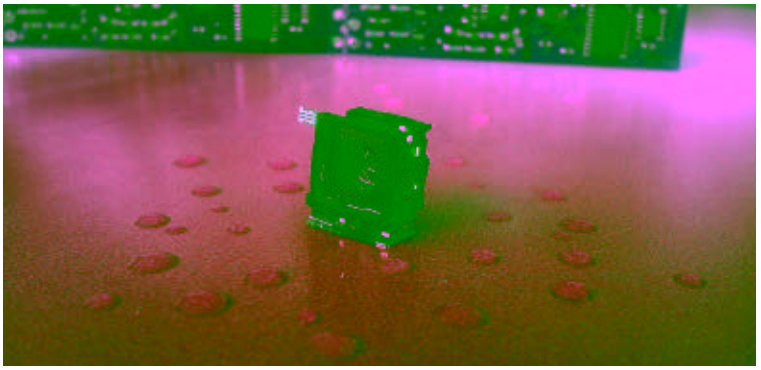
What cleaning procedures will achieve the required degree of cleanliness repeatably and efficiently for a specific electronic product? What are the possibilities offered by special procedures for cleaning and activation? Are there ways to carry out cleaning and conformal coating in a single process?

Answers to these and many other questions connected with cleaning of components and surfaces in electronics manufacturing are offered at parts2clean. The leading international trade fair for industrial parts and surface cleaning will be held from Oct. 22-24, 2013 at the exhibition center in Stuttgart, Germany, providing comprehensive details of cleaning systems, alternative cleaning technologies, cleaning media, quality assurance and test procedures, cleaning and transport containers, disposal and processing of process media, handling and automation, service provision, consulting, research, and technical literature.

The simultaneous German-English/English-German translation of lectures at the parts2clean technical forums provides a fund of knowledge about the industrial cleaning of components and surfaces. www.parts2clean.com



CO_2 snow-jet cleaning permits dry and gentle removal of films and particle impurities, for instance around wire bonds. The ease of automating this cleaning process allows it to be integrated as part of the bonding system. ***(Photo: ACP)***



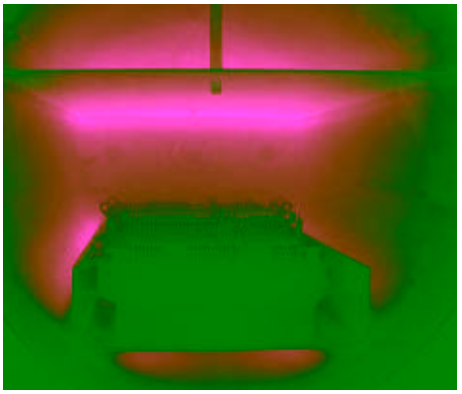
The demand for reliability and longer life span of electronic components put the focus back on cleaning in electronics manufacturing. ***(Photo: Puretecs)***

ties as a solvent upon a range of nonpolar impurities such as grease and oils. Supercritical CO_2 has low viscosity and low interfacial tension, resulting in improved ability to penetrate crevices. This enables cleaning of components with highly complex geometries such as tiny drilled holes. In electronics manufacturing this technology offers the ability to clean such items as complete PCBs and assemblies, removing flux residues and cleaning away oils and grease from metallic components such as contacts. It meets the requirement for an environmentally friendly, dry, and residue-free procedure.

Liquid carbon dioxide is also used as the medium in CO_2 snow-jet cleaning—in this case in the form of minute snow crystals. With its combination of chemical, thermal, and mechanical properties, the non-poisonous and non-inflammable CO_2 snow removes surface films and particulate contamination leaving no residue, and can also be used selectively on functional areas such as contact points. Since the cleaning is itself a dry process, there is no need for an energy-intensive subsequent drying procedure. The procedure is employed in the most diverse of applications in electronics manufacturing, such as in preparation for bonding processes, equipping PCBs and foil-PCBs, and in the manufacture of metal-insulator semiconductors (MISs).

Plasma: cleaning in the fourth state of aggregation

Plasma, a gaseous mixture of atoms, molecules, ions, and free electrons, allows efficient surface treatment of electronic parts and components of different materials, simultaneously cleaning away organic impurities such as oils and grease and activating the surface. This double function is based on a physical and chemical reaction during the procedure. Depending on the application in question, low-pressure plasmas or inline-capable atmospheric pressure plasmas can be used. With low-pressure plasmas, both oxidizing and reducing processes can be carried out. An oxidizing plasma can clean away organic contaminants such as grease, oil, and adhesive residue prior to soldering or bonding. A reducing plasma process can be used, for example, to improve bonded connections by reduction of electro-plated metallic layers. Surface cleaning and activation by atmospheric pressure plasmas are used in the electronics industry in such tasks as pre-printing, bonding, or casting of electronics boards and semiconductors, manufacture of opto-electronic components, and prior to wire-bonding.



Plasma cleaning permits efficient surface treatment of electronic parts and components of different materials. ***(Photo: Diener Electronic)***

Non-inflammable HFEs allow for reliable removal of flux residues with good results. ***(Photo: Puretecs)***

Doris Schulz has studied Business Administration at the Fachhochschule für Wirtschaft, Gestaltung und Technik, Pforzheim, Germany, and has worked with different companies in Public Relations. In 1995, Doris has founded her own PR consultancy, and she has also worked as a freelance journalist. One of her specialties is the field of surface treatment. doris.schulz@pressetextschulz.de

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Rapid Microbiological Methods

ATP bioluminescence combines two technologies, membrane filtration and fluorescent staining, to detect and quantitate micro-colonies.

Beth Ann Brescia
Microbiology Application Scientist
EMD Millipore Corp.
Billerica, Mass.

This article is excerpted from a book chapter on microbial methods to be included in Specification of Drug Substances and Products: Development and Validation of Analytical Methods, *to be published by Elsevier.*

Compendial microbiological methods have been in existence for many years, with only minor changes being incorporated. Such methods include U*nited States Pharmacopeia* (USP) Chapter <61> "Microbiological Examination of Non-sterile Products: Microbial Enumeration Tests"[1], USP Chapter <62> "Microbiological Examination of Non-sterile Products: Tests for Specified Microorganisms" [2], and USP Chapter <71> "Sterility Tests."[3] Recently, more rapid technologies have emerged and, in some cases, have received regulatory approval as alternatives to the traditional compendial tests.

Rapid microbiological methods

Alternative technologies are available for the rapid detection of microorganisms. In 2000, the **Parenteral Drug Association** (PDA) published the first guidance document on how to validate and implement alternative rapid microbiological methods.[4] The USP and *European Pharmacopeia* (EP) have also published guidances on alternative methods.[5,6]

EP 5.1.6 placed rapid microbiological methods (RMMs) into three categories: growth-based methods, direct measurement, and cell component analysis. Growth-based methods detect a signal after a short incubation period in liquid or on solid media; examples include detection of CO_2 production by colorimetric methods or a change in head space pressure and detection of adenosine triphosphate (ATP) by bioluminescence. Direct measurement methods can detect cell viability without requiring growth of the microorganism. One example of a direct measurement method combines fluorescent labeling and laser scanning cytometry to enumerate organisms. The sample containing microorganisms is filtered onto a membrane and treated with a combination of stains to fluorescently label viable organisms without the need for growth. The membrane is scanned by a laser, fluorescent light is detected, and a membrane scan map is produced which captures the position of each fluorescent event, which is then verified by visual examination using an epifluorescent microscope. The third type of RMM is cell component analysis or indirect measurement; expression of certain cell components correlates to microbial presence. One example is amplification of DNA or RNA by polymerase chain reaction (PCR). RMMs can be qualitative (presence/absence) or quantitative (enumeration), destructive or nondestructive, and can be applied to filterable or non-filterable products.

In 2006, the **FDA**'s **Center for Drug Evaluation and Research** (CDER) published a paper on the use of alternative microbiological methods.[7] The authors stated, "New microbiology methods can offer advantages of speed and precision for solving microbiological problems associated with materials or environmental influences. Neither corporate economics nor regulatory attitudes should be a barrier to the use of new testing technologies or different measurement parameters."

Rapid sterility test methods

Sterility testing has also undergone an evolution. It was first introduced in the 1930s for testing of liquid products (USP XI) as a seven-day test using one medium at 37 °C targeted for human pathogens. By the early 1940s, an incubation temperature of 22 to 25 °C was added specifically for yeasts and mold with a 15-day incubation period. By the mid-1940s, a sabouraud-based medium was used for ten days instead of 15 days and fluid thioglycollate medium (FTM) for seven days. In the mid-1960s, the incubation conditions for FTM changed to 30 to 32 °C for seven days. Several changes were incorporated into the test in 1970, including different incubation times for aseptically filled products (14 days) versus terminally sterilized products (seven days), incubation temperature ranges were increased to 30 to 35 °C for FTM and 20 to 25 °C for soybean casein digest medium (SCDM), and the incubation period was used to differentiate the membrane filtration test (seven days) from the direct inoculation test (14 days). Over the course of several years, efforts led to incubation times being harmonized to 14 days in 2004, and by 2009 (USP 32) the remaining portions of the sterility test were harmonized with only a few exceptions.[8]

Use of a rapid method as an alternative to the traditional sterility method requiring 14 days has several advantages. A shorter incubation minimizes the time needed for recovery of microbial contaminants, enabling more rapid implementation of corrective actions that would prevent cross contamination to other product batches and can reduce product release time.

The FDA's **Center for Biologics Evaluation and Research** (CBER) has evaluated three growth-based rapid sterility methods: two qualitative methods utilizing CO_2 monitoring technologies and one quantitative method incorporating ATP bioluminescence technology. A total of 14 different

microbial strains (ATCC and environmental isolates) representing bacteria (Gram negative, Gram positive, aerobic, anaerobic, and spore forming), yeast, and fungi were used. The sensitivity of the rapid microbiological methods was compared to the compendial membrane filtration (MF) and direct inoculation (DI) methods with regard to observation of growth at various low levels of inoculations. Results showed that the ATP bioluminescence technology was the most sensitive of the methods, the CO_2 monitoring technologies were more sensitive than the compendial methods, and the compendial membrane filtration method was more sensitive than the direct inoculation method.[9]

In 2010, a leading pharmaceutical company implemented a rapid sterility method consisting of a five-day incubation as compared to the traditional 14-day incubation. The ATP bioluminescence technology system was selected because it is growth based, uses membrane filtration which is similar to the compendial method, and can detect one colony-forming unit (cfu) following incubation.[10]

The system uses ATP bioluminescence to detect and quantitate micro-colonies. The first step is to filter a sample through the system's filter unit and place the membrane onto a solid media cassette. The media cassette is incubated to allow for the formation of micro-colonies and the detection of ATP. The filter is removed from the media cassette and sprayed with an ATP releasing agent that makes the cell wall of the microorganism permeable to ATP. A bioluminescent enzyme reagent is then applied, which reacts with the ATP to produce light (photons). The membrane is moved to the detection tower where image processing takes place. The photons are converted into electrons and multiplied in the photomultiplier tube (PMT). The location of the photons correlates with the location of the micro-colonies. The image forms on a charge coupled device (CCD) camera, a computer algorithm then processes the data and enumerates the micro-colonies in colony forming units (CFUs), and a 2D and 3D image map is generated.[11]

Taking into consideration the compendial guidelines (USP Chapter <1223>, Ph. Eur 5.1.6), the pharmaceutical company validated the rapid method and was able to demonstrate that it delivered robust, reliable results. Equivalent performance to the compendial sterility test method in terms of robustness, ruggedness, repeatability, limit of detection, specificity, accuracy, and precision was reported. In 2010, the company achieved regulatory approval by the FDA, **EMA**, and **MHRA** to use the alternative method in lieu of the compendial method.[12]

Rapid bioburden methods

Quantitative rapid methods can be used as alternatives to the traditional bioburden test. The ATP bioluminescence technology system combines two proven technologies: membrane filtration and fluorescent staining. Membrane filtration is the standard method for microbial bioburden testing due to the capacity to remove any inhibitory agents and the ability to process larger volumes. After filtration and a short incubation time (approximately one-third shorter than traditional incubation times), reagent is applied to the membrane and any viable and culturable microorganisms retained on the filter are stained with a fluorescent marker. The active microbial metabolism of the microorganism causes an enzymatic cleavage of the non-fluorescent substrate and, once cleaved inside the cell, the substrate liberates free fluorochrome into the microorganism cytoplasm. As fluorochrome accumulates inside the cells, the signal is naturally amplified. The cells are then exposed to the excitation wavelength in the system's reader to visually counted.[13]

Validation of alternative methods

USP Chapter <1223> states, "Validation studies of alternate microbiological methods should take a large degree of variability into account. When conducting microbiological testing by conventional plate count, for example, one frequently encounters a range of results that is broader (%RSD 15 to 35) than ranges in commonly used chemical assays (%RSD 1 to 3). Many conventional microbiological methods are subject to sampling error, dilution error, plating error, incubation error, and operator error."[5] The USP goes on to state that the characteristics such as accuracy, precision, specificity, detection limit, quantification limit, linearity, range, ruggedness, and robustness are applicable to analytical methods and less appropriate for alternate microbiological method validation. Yet, the general present regulatory expectation is to apply these analytical performance characteristics to alternative rapid microbiological method validation. Additionally, USP includes these validation parameters in Chapter <1223>.

It is more than appropriate for vendors of new alternative technologies to apply these analytical performance characteristics during validation. The data generated from the validation testing should be analyzed using statistical tools to show that the method meets the applicable requirements. However, once the technology is validated, the end user should not have to repeat the in-depth validation that was conducted by the vendor. Rather, the end user should focus on whether or not the alternate method will yield results equivalent to, or better than, the results generated by the conventional method when testing their product.

In 2011, FDA CDER published *A Regulators View of Rapid Microbiology Methods*[14] and stated, "While it is important for each validation parameter to be addressed, it may not be nec-

essary for the user to do all of the work themselves. For some validation parameters, it is much easier for the RMM vendor to perform the validation experiments." The author goes on to say that the end user would still have to perform their own studies not addressed by the vendor, which include product specific data.

A RMM may incorporate portions of the compendial test up to a certain point. For example, a sample may be processed using conventional membrane filtration and the membrane placed on a recovery medium and incubated. However, at that point the presence of viable cells may then be demonstrated by use of some alternative rapid technology. Hence, validation would be required on the recovery portion of the method rather than on the entire test.

When evaluating the range of the method, the vendor needs to ensure that the upper end of the range is challenged. New technologies that enumerate micro-colonies verses macro-colonies can count a higher population. Traditional pour plate or membrane filtration methods are limited in the numbers of macro-colonies counted, with 300 cfu being the maximum number. New technologies can count much higher cfu in some cases.

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EMD Millipore has developed the Milliflex® Rapid Microbiology Detection System, intended for the rapid detection, response, and resolution of microbial contamination in filterable samples throughout the manufacturing process.

INDUSTRY EVENTS

July 9-11
SEMICON West
From silicon to software to systems, SEMICON West showcases technology companies from across the micro-electronics supply chain and beyond. This event brings together the people, companies, technologies, and ideas that drive the electronics revolution.
San Francisco, Calif.
www.semiconwest.org

July 23-24
Risk Assessments for Cleanrooms and Controlled Environments
The Institute of Environmental Sciences and Technology will host a course to train cleanroom professionals in the various risk assessment methods available, with time set aside to practice using these tools.
Arlington Heights, Ill.
www.iest.org

July 29-31
American Glovebox Society Annual Conference
This conference will exhibit products and services to those who purchase and use them.
Lake Tahoe, Nev.
www.gloveboxsociety.org

September 4-6
SEMICON Taiwan
Connect with the companies, people, products, and information shaping the future of design and manufacturing for semiconductors, nanoelectronics, MEMS, photovoltaics, and related advanced electronics.
Taipei, Taiwan
www.semicontaiwan.org

September 8-13
EOS/ESD Symposium & Exhibits
The EOS/ESD Symposium is the international technical forum on electrical overstress and electrostatic discharge that features research, technology, and solutions to increase understanding, enhance quality and reliability, reduce and control costs, and improve yields and productivity.
Las Vegas, Nev.
www.esda.org

September 10-11
SPIE Photomask Technology 2013
The 33rd Annual SPIE Photomask Symposium, organized by SPIE and BACUS, the International Technical Group of SPIE, provides the forum to present the newest findings, discuss trends, solutions, and their effects on the semiconductor lithography.
Monterey, Calif.
www.spie.org

September 16-18
PDA/FDA Joint Regulatory Conference
Each year, FDA speakers provide updates on the current state of efforts impacting the development of global regulatory strategies; while industry professionals from pharmaceutical companies present case studies on how they employ global strategies in their daily processes.
Washington, D.C.
www.pda.org

October 2
ISPE Boston Product Showcase
With an attendance of over 2,000 professionals from the biopharm industry, this is the biggest one-day gathering of biotechnology and pharmaceutical professionals in the Northeast.
Foxborough, Mass.
www.ispeboston.org

Access Control in Cleanrooms

Interlocking door systems and appropriate access options minimize contamination via entry points.

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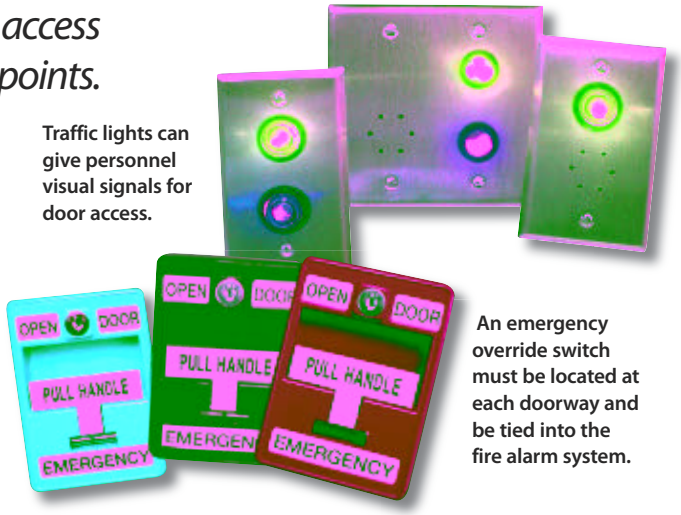
When cleanrooms are used in manufacturing or scientific research, the doors and framing materials must have proper gaskets and seals to not allow contaminated air in or out of the area, and the door hardware must close and reseal after each personnel passage. However, additional door devices—such as card access systems, electric locks, station controls, and traffic lights—may be necessary to limit access to authorized persons and operate the airlock for environmental conditions.



Traffic lights can give personnel visual signals for door access.

An emergency override switch must be located at each doorway and be tied into the fire alarm system.

Access conditions and options

In order to seal the cleanroom and also allow access to personnel, vestibules with two or more doors are constructed and only one door is allowed to be opened at a time. A simple two-door airlock will have electric locks on each door—opening either door will cause the other door to lock. The door hardware must cause the doors to close immediately after an entry or exit. If both doors are accessed simultaneously, it will be impossible to prevent possible contamination through the unsealed doorway. One solution is to have one or both doors normally locked. Access can be granted through a locked door by card access or push button controls located adjacent to the door and within arm's reach.

Frequently, the construction and/or locations of interlocked doors do not allow visibility of the other controlled doors. Traffic lights can be used in these situations to allow a smooth entry and exit by personnel. A normally unlocked door will have an indicator that turns red when the door is locked. If the door is normally locked then the light should be green to indicate that access is allowed. PLC-based controllers can easily provide this function, but most relay logic interlocks cannot. Large, hi-intensity LEDs are best for these applications and operate for an extended life cycle.

If a door does not fully close, then the other related doors will be inhibited and not allow entry or exit. A door prop alarm function may be incorporated into the PLC programmed logic or can be an independent stand-alone alert device. The door prop function monitors how long the door remains opened—should it not be closed in a predetermined time, an alert is sounded and a supervisor may be summoned.

Overrides for safety

Special lock override controls may be included to allow escape in an emergency. The system must be tied into the fire alarm system to unlock the doors in case of fire. An emergency override switch should be located within the room and at each doorway. Some facilities use an emergency pull station or a latching push-pull switch with a key reset; these devices frequently incorporate a built-in sounder to alert area personnel that the doors are unlocked.

Custom cleanroom sequences

Some facilities require automatic door operators to allow rolling carts. Most swing door operators are powered open and spring closed. Sliding doors are nearly always powered open and power-closed. If locks are needed, special programming is required to have the door sequenced to unlock before the door operator attempts to open it. Traffic can be directed by specifying motion sensors and/or push button control switches on only one side of the doorway.

Complex traffic patterns can be accommodated using a PLC-based controller. These can involve dozens of doors, or doors used to pass between two sterile rooms. This situation requires that all doors in each of the two rooms be secured whenever the "shared" door between them is open. The shared door may be normally unlocked for faster traffic if the other doors in the two rooms are normally locked.

A PLC programmed interlock can operate devices and systems other than electric locks. A custom timing sequence may be required to allow exhaust fans to extract contaminated air from the airlock before allowing the door to be unlocked. Similarly, one system uses a special function to inflate and seal the door gaskets before allowing access through another door.

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Performing a Clean

For ISO-5 clean zones, USP 797-compliant testing includes determining if

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As a Registered Cleanroom Certification Professional, I have seen an increase in the use of "clean zones" inside of cleanrooms in pharmacies. There are numerous types of unidirectional-flow devices that have been used in the past; however, when using a unidirectional-flow device in the compounding processes, the suppliers, customers, and certifiers need to keep in mind the meaning of the direct compounding area, first air, and critical site.

• Direct compounding area (DCA): a critical area within the ISO Class 5—a primary engineering control (PEC) where critical sites are exposed to unidirectional HEPA-filtered air, also known as first air.

• First air: the air exiting the HEPA filter in a unidirectional air stream that is essentially particle-free.

• Critical site: a location that includes any component or fluid pathway surfaces (e.g., vial septa, injection ports, beakers) or openings (e.g., opened ampoules, needle hubs) exposed and at risk or direct contact with air (e.g., ambient room or HEPA filtered), moisture (e.g., oral and mucosal secretions), or touch contamination. Risk of microbial particulate contamination of the critical site increases with the size of the openings and exposure time.

To test a clean zone, there are several issues like smoke reflux, dead spots, and numerous smoke deviations to look for. It is important not to separate the media filter from the wall since the farther it is from the wall, the more reflux can be found. The HEPA filter media should be flush with the walls of the clean zone and the front shield. The lexan shield must be consistent in its area of opening from the HEPA filter through the entire travel of the ISO-5 zone. Providing an incline to expand the area of the opening will lower the velocities and uniformity of the supply velocity. The uniformity of airflow velocity can be affected by the type of filter utilized, like a room side replaceable HEPA or ULPA filter. The typical loss of filter area also lowers the cfm (cubic feet per minute) of the filter, thus lowering the velocities as well as the volume.

To perform this test personally, I have taken 10 measurements (two columns, five rows) of velocity (testing a 2 by 4 ft. HEPA filter) using a termo-anemometer held by a suitable stand to avoid the manual fluctuations.

The test procedure to validate these clean zones requires a thermo-anemometer with a ring stand placing the probe of the anemometer 12 in. under the filter and beginning 6 in. away from the corner in each direction. Then a 12 in. grid is set up with readings taken every 12 in. on center.

Compute the arithmetic mean of the velocities recorded. Ex. average x = (y1 + y2 +…+ yn /n).

Where:
y= Average of each test position
n= Number of test positions
x = Average of filter face velocity
Compute the standard deviation $(S)^2=((y1 - x)^2 + (y2 - x)^2 + ….+ (yn - x)^2) / (n-1)$
Compute the relative standard deviation (RSD)= (standard deviation (S) / average velocity (x)) * 100

Most compounding pharmacy clean zones have I.V. bars and bags which makes it important to get the relative standard deviation as low as possible. IEST-RP-CC-002.3 Section 6.1.1 states, "The maximum relative standard deviation is typically 15% when using an electronic micro-manometer with multi-point probe."

It's preferable to keep the RSD below 10% to create the effect necessary to pass the smoke challenge without high reflux, dead spots, or airflow that travels sideways as opposed to straight down.

Selecting the filters for the clean zones

Careful consideration of filter manufacturers is recommended as we have seen large discrepancies in uniformity of face velocities among different manufacturers and even filter types, like HEPA to ULPA designs. Uniformity or unidirectional flow is the key to the functionality of these systems as well as a continuous low level return beneath the work zone.

Achieving a deviation of less than 14 degrees in an ISO-5 clean zone

There must be a continuous length of HEPA filter across a wall away from the door with a 4 in. continuous wall return cavity along the back of the area. The clean zone must have 100% coverage of the area, and use a polycarbonate directional flow shield from the ceiling grid to 5 ft. off the floor. The work table or zone should be moved nearer or farther away from the back wall as necessary to cause a waterfall effect on the front and back edges of the work table. A solid table produces an effect similar to a biological safety cabinet centerline smoke split. (Note: Perforated tables are difficult to clean and maintain.) Be sure the table is no more than

Zone Smoke Test

airflow conforms to design criteria.

30 in. in height and 30 in. or less in width. Once the desired water fall effect is noticed, secure the work table at that location and perform the smoke pattern test.

Performing the clean zone smoke pattern test

Purpose: This test determines that the airflow within the clean zone conforms to the manufacturer's design criteria. This shows the airflow within the DCA moving in a downward direction with no dead spots or refluxing in the critical site. Be sure that the ambient air does not enter the clean zone or other areas except through the supply HEPA filter. Once the air enters the DCA, it must move to the returns without reentry. (Note: This test should be performed following completion of the airflow velocity, volume, room air changes per hour, room pressures, and uniformity tests.)

Apparatus: A source of visible smoke that is generally neutrally buoyant. Chemical smoke tubes or glycol-base smoke generators are examples of acceptable smoke sources.

Good results can be achieved using a theatrical fog generator that has a mixture of glycol with a fan speed controller connected to a delivery tube, supported by a hands-free stand (1 in. diameter PVC with small holes to create a laminar-like curtain smoke pattern). It is recommended that the PVC tube be the same size as the distance between the front shield and the wall.

- Adjustable support stand
- Plumb bob
- Tape measure
- Video or digital camera

Procedure:

- Place the delivery tube with the plumb bob.
- Turn on the smoke generator and adjust the fan speed-control to get the desire laminar airflow.
- Introduce the aerosol stream isokinetically and, as nearly as practical, isothermally.
- Generate the smoke remotely from the vicinity of the source.
- Move the smoke tube through the entire area to be tested, sliding the hands-free stand slowly so that the whole clean zone area is observed and video recorded.
- With the pointer mounted in the support stand, at the work table exit plane, measure the offset distance (Δs) between the theoretical straight-line flow point and the center of the source stream. Measure the distance between the delivery outlet tube and the work table exit plane (d).
- Calculate the angle of deflection, Theta (θ). The angle (θ) is found as the arctangent of the ratio expressed as $(\Delta s)/(d)$ using the equation: $\theta = \text{Arctangent}(\Delta s)/(d)$.
- Example: if the distance between the delivery outlet tube and the work table (d) is 4 ft. and the offset distance (Δs) between the theoretical straight-line flow point and the center of the source stream is 1 ft. Using the equation, we have θ = Arctangent (1 ft./4 ft.).
- θ = Arctangent 0.25.
- $\theta = 14.036°$. That means that for every 4 ft. (d) we will have no more than 1 ft. (Δs).

Acceptance: Readings in excess of a 14-degree offset should be discussed with the customer and either approved or corrections made until acceptable.

The clean zone smoke pattern test needs be performed "as built," "at rest," and "operational" phase.

Other tests that need be performed are: airflow volume, airflow velocity, and uniformity test; HEPA filter leak test; airborne particle count test; rooms pressurization test; light level and uniformity test; noise level test; temperature uniformity test; moisture uniformity test; vibration test; microbiological sampling test and air changes per hour (ACPH) calculations. (See IEST-RP-CC-006.3 Section 5.1 and USP 34 (1116) for details.)

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HVAC Strategies for the Cleanroom

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What are some key points in HVAC engineering for cleanrooms?

"Good things, when short, are twice as good." *~Baltasar Gracián, The Art of Worldly Wisdom, translated from Spanish*

A dilemma

This month's topic poses a dilemma. The HVAC system in any controlled environment is the kingpin of clean. Given its criticality, and the myriad considerations in engineering an HVAC system for a cleanroom, this column could end up rivaling *War and Peace*. To save your sanity (and mine), I decided old Baltasar must be right, so following is the CliffsNotes version, touching on some of my favorite topics. Just remember to consult your favorite engineer when undertaking your next project for "the rest of the story."

Some grounding

When it comes to cleanroom HVAC, it's all about contaminants and environment control. The nasty "C-word" lurks everywhere. Contaminants — invisible to the eye—can pack a punch and wreak havoc on product yield and integrity if not controlled. This sets up a potential double whammy: hitting the company's yield and bottom line, or a research team's multi-year effort.

The optimal HVAC design solution is determined by desired temperature and humidity control, air flow and pressure, and filtration requirements and air change rates, among other considerations. These design factors are dictated by the requirements unique to your process, facility, and regulatory requirements.

Whether creating a controlled environment for an electronics manufacturer or a life sciences environment free of pathogens, the HVAC system controls your success and will significantly impact your operating costs.

Contamination lurks everywhere

Whether your goal is to create an environment at ISO 9 classification—not tremendously different from outside air—or drive the cleanliness to ISO 1, the most stringent of controlled environments, a few fundamentals apply:

- Contaminants are not your friend—start by not allowing them in from the outside.
- Those that infiltrate your environment must be eliminated quickly—don't let them accumulate or hang out. Your cleanroom is not the neighborhood bar.
- Besides worrying about particulate interlopers from the outside environment, make sure you have your own house in order. This means minimizing contaminants that your manufacturing or research processes—including the equipment integral to your operations—throw off, whether through biological, chemical, or operating processes. And make sure your employees consistently follow protocols developed to minimize contamination.

A tool you can use: Computational Fluid Dynamics (CFD) analysis

CFD is a software modeling tool that can provide an accurate view of both existing airflow conditions while also modeling projected airflows of a variety of HVAC solutions or system adjustments. CFD is a precise and valuable tool both to design new controlled environments and also to diagnose and solve problems in existing cleanrooms.

CFD can trace its roots to the 1930s, when two-dimensional models were developed to solve linearized potential equations. The development and continued advancement of computing not only enabled the analysis and modeling of any gas or liquid fluid flow in 3D, but also enabled analysis of complex equations. Los Alamos National Labs lays claim to being the first to use computers to model fluid flow using the Navier-Stokes equations.

A valuable tool for today's controlled environments engineer evolved from that rich history. Not only can CFD modeling assist in selecting the most efficient and effective air handling system when designing a new controlled environment, it is extremely useful in dealing with underperforming or problematic controlled environments. CFD can analyze airflow problems, humidity issues related to airflow, temperature gradient issues, the impact of tool sets and other equipment on airflow, and identify air pressure differentials throughout a space or track contaminant flow. This analysis is priceless when working to identify root causes of underperforming cleanrooms.

Figure 1 shows CFD modeling of a Class 1,000 cleanroom that was experiencing inconsistent airflow and stagnation issues, while the "after" shot in Figure 2 validates the effectiveness of the solution.

Energy is king in the HVAC kingdom

Cleanrooms rank among the top energy consuming facilities in the world, driven in large part by their HVAC requirements to meet stringent airflow and pressurization requirements within strict temperature and humidity controls. And as existing technologies increase in sophistication and new technologies create additional demand, controlled environments have proliferated around the globe in more than 30 different industry sectors and are a mainstream feature of academic, medical, industrial,

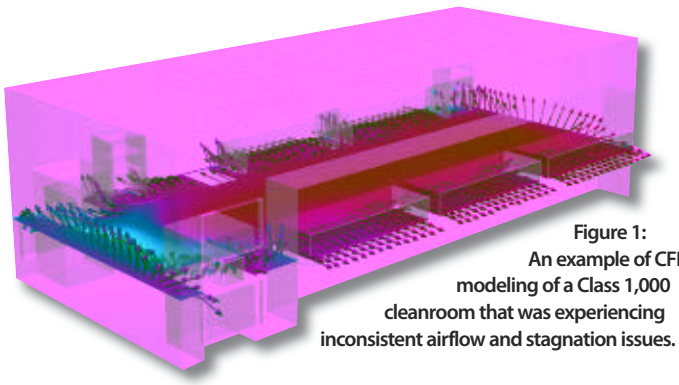

Figure 1: An example of CFD modeling of a Class 1,000 cleanroom that was experiencing inconsistent airflow and stagnation issues.

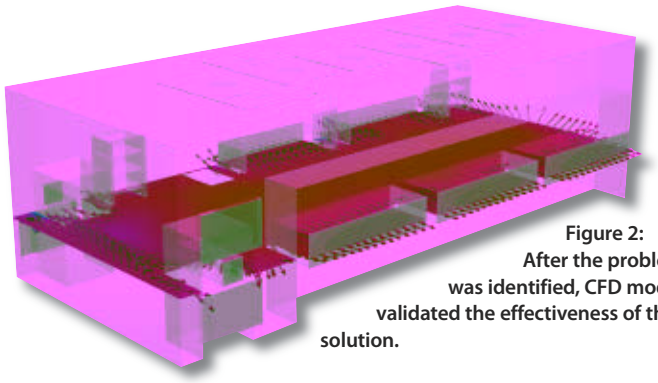

Figure 2: After the problem was identified, CFD modeling validated the effectiveness of the solution.

and defense research facilities. It's been estimated that cleanrooms demand between 10 and 100 times more energy than standard office spaces—mainly driven by air cleanliness standards—and the HVAC system can account for more than half of the facility's energy costs. This impacts operating costs, on top of an already costly capital facility.

Following are a variety of strategies to help reduce energy costs related to your HVAC system:

1. To begin, minimize demand. Take a look at your building. Can you increase the efficiency of the shell? When building new, carefully orient and develop the building form. Is there an opportunity to reduce the volume of your cleanroom? Less volume equates to less air re-circulation with resulting HVAC savings.

2. Make sure you accurately scope the level of cleanliness and the square footage required. Going overboard in either category will drive up your costs. Considering reducing positive pressurization where prudent.

3. Flexibility is key. Design your HVAC system with an eye towards flexibility, not only for sustainability, but for future product line and expansion capabilities as well. Don't forget to plan your HVAC equipment to accommodate part load scenarios.

4. Subdivide your facility's space classifications. Carefully examine the proposed process and product requirements when determining your required cleanroom classification. Don't shoot an ant with an Uzi. Do you really need the entire space to be stringently controlled?

5. Mini- and micro-environments are your friends; stick or prefab? Consider the use of micro- or mini-environments (see the May 2013 issue of *Controlled Environments)* and a mix of stick built and prefabricated areas—determined by process specifications and flexibility needs. Utilize these tools to meet your process requirements instead of upgrading your entire cleanroom.

6. Invest in high efficiency equipment. Your upfront costs are an investment with surprisingly short payback periods. And don't forget to use high efficiency filters.

7. Consider energy recovery and waste recovery strategies. Energy recovery strategies such as an exhaust energy recovery system, co-generation, and equipment or other heat recovery systems can cut demand and costs.

8. Use alternate energy appropriately. You can reduce the load on your HVAC system by carefully analyzing and appropriately using alternative energy sources throughout your facility. Consider solar heating and power, daylight, wind energy, and thermal where technically sound and fiscally responsible. "Green for a reason" is the mandate at SMRT, ensuring that alternate energy sources are operationally sound, financially responsible, and appropriate to the application. Don't let anyone sell you on being green for green's sake.

9. Analyze the viability of reducing air change rates (ACR). The sizes of your motors and fans are driven in large part by the air change rate in your cleanrooms. Larger motors and fans drive increased HVAC investment and operating costs. You can reduce power usage by approximately two-thirds if you reduce your ACR by approximately one-third.

10. Adjust your airflow to match your production load. Scheduling software and timers can be used to decrease air recirculation and the HVAC load during periods of reduced production. Ditto the wonders of occupancy sensors that can make automatic adjustments depending on the occupancy levels of your biggest contaminant source—people.

11. Locate equipment outside the cleanroom where appropriate. This is a triple bonus strategy. When you locate process tools in an adjacent chaseway and provide critical clean access on the cleanroom side, you will reduce heat gain as well as the square footage required in your cleanroom, resulting in less demand on the HVAC system. You will also make future equipment maintenance easier and less costly.

12. Use variable frequency drives (VFDs). Variable frequency drives, which adjust HVAC equipment speed to match conditions, can cut your energy up to a third compared to constant speed drives.

13. Use particle counters to manage airflow in real time. Carefully located optical sensors provide 24/7 particle counts to the building management system, allowing the HVAC system to operate with efficiency matched to need.

14. Analyze your air distribution system to reduce pressure drop. Your HVAC fans have to work harder in a restrictive air distribution system, raising energy consumption. Keep the freeway open with straight ductwork where possible, eliminating obstructions and carefully sizing duct diameters. Consider the pressure drop properties of supporting equipment like coils, fans, and filters.

15. Don't be overly conservative or cautious. Don't overdesign your HVAC system, or build in too many safety nets. Those behaviors compromise operating efficiencies.

A final word

The world of HVAC design for controlled environments is an always-evolving field with new equipment and constantly emerging operational innovations. While this article provides an overview of some key considerations, the unique properties of your process, product, or research requirements—coupled with those of your physical plant—will determine best practices.

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Clean Space Without a

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Manufacturers often ask how to achieve a clean space without using a cleanroom. There are many reasons to do this, including achieving a reasonable process flow and assuring economic competitiveness. A clean space involves basic design and structure. There is an initial capital outlay for micro-environments and facilities design. Achieving a clean space involves coordinating engineering planning and production activities with the facilities group, the customer, and with safety/environmental professionals. Employee practices may also have to be addressed.

The first question, albeit a semi-dramatic question, is: what is my motivation? There are many reasons for setting up a clean area outside of a formal cleanroom. Do you need clean air? Clean water? Clean process chemicals? Product protection? Worker protection? Customer satisfaction? An actual clean area? The perception of a clean area?

What does the customer expect?

Where particles in the air must be controlled, some sort of HEPA filtration is required. If the customer has formal or contractual requirements for a cleanroom, building a cleanroom is the only way to proceed. In other instances, a mini-environment may be a more economical and technically-superior approach.[1] A mini-environment where the processes are conducted by observant, well-educated personnel can be more successful than a stand-alone cleanroom where general employee practices are not as well defined.

However, there are also perceptual and expectation requirements. These requirements may first appear during a site inspection by a prospective customer. One group took what appeared to be the logical step of adopting a bench with filtered air flow for final cleaning prior to the final finishing process. The prospective customer was not impressed. The expectation was the presence of a clean environment that looked like an independent room.

Humble beginnings

Aside from customer perception, it is important to define the clean space, to define the contamination sources, to define how the product might become contaminated; this means starting with what some may consider to be the non-glamorous, mundane parts of cleaning and contamination control. We often assert that contamination control starts early-on in the assembly process. This means that, for example, the machine shop may require clean areas and clean practices.

Initial critical cleaning

Immediate cleaning after machining is one of the most effective paths to achieving product quality. Since cleaning involves three steps (washing, rinsing, and drying), it is crucial to assure that these steps are carried out promptly and effectively.

Initial cleaning processes typically do not require the complexity of a multi-stage precision cleaning system with ultrasonics. Benchtop cleaning may use a simple immersion bath or a spray system. Unfortunately, the cleaning products that are used may be poorly-controlled or may even be unspecified—the process is inherently considered to be unimportant. Household, consumer products may be used. A safety or environmental professional may decree a change in the cleaning chemistry, perhaps with admirable air quality or worker safety motivations. However, if the required cleaning efficacy is not achieved, undesirable (sometimes catastrophic) impact on product quality has been observed. Defining a clean area may start in the machine shop; this means that the processes have to be specified at the engineering level.

Applicators, peripherals, environmental controls

A rag is not just a rag. Handwipe cleaning often involves application of the cleaning agent using brushes, cloth, or paper towels. To achieve a clean area, you have to specify the appropriate applicator. This is always a compromise because applicators inherently introduce some level of particulate or chemical contamination.[2] Achieving a clean area in a shop involves specifying the applicator for the cleaning agent.

Evaluate gloves and other protective equipment. Particularly at non-cleanroom stages of production, the Industrial Hygienist may be in charge of specification. Of course the worker has to be protected. However, product contamination also has to be minimized. As an engineer or process designer, the ball has to be in your court as well; so you may need to coordinate (i.e. negotiate) with the safety professionals.

Drying and storage

Often, parts are dried using shop air. This air may contain oil; and the net result of attempts at drying may be deposition of both thin film and particulate contaminants. Coordinating with the facilities group and monitoring shop air is an important step in achieving a clean area.

Storage and transport

Parts may be machined and then stored either in the shop or in a storage room where air quality and access are not controlled. If parts are stored in a shop, there can be gradual accumulation of process fluids, dust, and other soils; and there is a tendency to move the parts from place to place. Set up a protocol for protecting and storing the parts after they have been machined and cleaned.

Cleanroom

Invest in an enclosed storage space, specify that parts be stored in that space immediately after cleaning, and limit access to that space. Even a simple enclosed, clearly-identified clean space can improve productivity. It can also improve customer perception.

Multi-purpose environments

We think of controlled environments, particularly of mini-environments, as protecting the product. However, mini-environments may have other purposes; and those purposes may conflict with product protection. For example, we want to keep contaminants away from the part. However, minimizing worker exposure to airborne hazards involves different airflow patterns than are used in product protection. Meeting community exposure and environmental requirements may result in containing the chemical within the manufacturing plant. Some booths and mini-environments are being designed to be multi-functional, to protect workers, the environment, and the product. As a process designer, or as the person involved in contamination control and process improvement, it is productive to interface early on with safety and environmental professionals as well as with facilities engineers. Taking a holistic approach to selecting the appropriate mini-environment is likely to lower the initial overall capital outlay and will result in less cumbersome processes.

Cleanroom style

Even if a formal access controlled and highly filtered cleanroom is not a requirement, consider the functions that a cleanroom provides when planning a clean workplace. Look at how product can become contaminated. Observe such factors as air flow, personnel practices, and proximity of contaminating sources.

Simple, low cost changes can make a big difference. For example, covering street clothes with a lab smock and providing a closet to remove fuzzy sweatshirts and jackets from the work environment can go a long way towards promoting the perception and actually achieving a cleaner working environment.

References

1. B. Kanegsberg and E. Kanegsberg, "Controlled Mini-Environments," *Controlled Environments Magazine,* August 2006.
2. Howard Siegerman, "Wiping Surfaces Clean," Vicon Publishing, 2004.

Barbara Kanegsberg and Ed Kanegsberg (the Cleaning Lady and the Rocket Scientist) are experienced consultants and educators in critical and precision cleaning, surface preparation, and contamination control. Their diverse projects include medical device manufacturing, microelectronics, optics, and aerospace. Contact: info@bfksolutions.com

Industry NEWS

Bischof + Klein Adds Production Cells to Class 5 Cleanroom

Bischof + Klein, a packaging and film specialist based in Lengerich, Germany, has added additional production cells to its Class 5 cleanroom. The company offers flexible packaging solutions for medical products and pharmaceuticals in this purity class.

The cleanroom production facility has been extended to cover over 8,800 ft². The production cells, including a module with a high-performance automatic punching machine, are connected to an intermediate warehouse. This machine produces single- and two-ply Tyvek cover sheets for the disposable syringe industry. The adjacent packaging line enables the bundle's initial protective packaging to be applied fully automatically. The closed-loop cleanroom chain includes a laboratory as well as lines for extruding polyethylene films and for converting sacks and bags. The personnel air lock has also been extended.

Materion Breaks Ground on Class 1,000 Cleanroom

Materion Barr Precision Optics & Thin Film Coatings has initiated the construction of a 3,000 ft² Class 1,000 cleanroom outfitted with infrared coating chambers and 3D patterning equipment. The work cell will enhance Materion's capability to manufacture low-defect coatings in high volume for the infrared wafer level, defense, and consumer electronics markets.

The Wafer Level Coating Cell, located at Materion's facility in Westford, Mass., is designed to be self-contained with a semiconductor manufacturing layout to handle 200 mm wafers. The multi-million dollar investment will assist in decreasing the cost of uncooled micro bolometer detectors and ultimately facilitate major growth throughout the commercial infrared camera industry. The Wafer Level Coating Cell enhances competencies across many other technologies such as gesture control filters, arrays, and gas sensing filters.

Completion of the work cell is expected in the third quarter of 2013 and will include a 3D photolithography deposition tool, semiconductor wet etch and alignment processing tools, semi-automated inspection tools, and several custom-designed high-volume 200 mm coating deposition chambers. The long-range plan foresees a total of 20,000 to 40,000 wafers per year when fully built out. Initial work will be composed of multiple volume production lines along with current projects aimed at the defense, commercial infrared, and consumer electronics markets. In addition, Materion is continuing to invest in its coating technology for the next generation micro-bolometer devices (less than 12 micron) and plans to unveil this new technology in 2014.

Materion Barr Precision Optics & Thin Film Coatings provides technologies including optical filters, filter arrays, lens coatings, and optical thin film component assemblies. Markets are composed of life sciences and medical, commercial, defense, thermal imaging, automotive, and space, science, and astronomy industries.

Catalent Pharma Opens Single-Use Biomanufacturing Center

Catalent Pharma Solutions, a provider of drug and biologic development services, delivery technologies, and supply solutions, has opened its biomanufacturing Center of Excellence in Madison, Wis. The new facility will quadruple Catalent's current biologics manufacturing capacity, allowing the company to extend its offerings in the sector while enhancing the efficiency and output of its GPEx cell line engineering technology as well as other mammalian cell lines.

The official opening follows Catalent's acquisition of an exclusive license to market Redwood Bioscience's SMARTag precision protein-chemical engineering technology for the development of advanced antibody drug conjugates (ADCs). Redwood's site-specific protein modification and linker technologies enable the generation of homogenous bioconjugates engineered to enhance potency, safety, and stability. Catalent's GPEx cell line expression system is intended for the rapid development of stable, high-yielding cell lines, and a broad range of analytical and fill-finish services.

Designed for flexible cGMP production, from 10 up to 1,000 L, and non-GMP production up to 250 L, the facility features extensive use of single-use technologies and unidirectional flow to greatly reduce cross-contamination risk. Manufacturing is supported by integrated analytical, formulation development and viral clearance capabilities, small-scale and large-scale process development laboratories, and separate microbiology and quality control functions.

Catalent is headquartered in Somerset, N.J.

Wayne State University Opens Cleanroom Lab for R&D

Wayne State University in Detroit has announced an initiative to increase and diversify microtechnology research at its multimillion dollar Nano Fabrication Core Facility (nFab). The cleanroom lab, which was originally built to focus on automotive applications, has been home to a broader set of nanotechnology research and development by WSU faculty and students. WSU has re-launched the lab and opened it to researchers, students, and companies throughout the region, who would otherwise not have access to the rare microfabrication environment, with a valuation exceeding approximately $12 million.

The nFab lab, located in the College of Engineering, was originally established in 2002 thanks to a major contribution from Delphi. Its mission is to create devices that benefit humanity. The lab provides researchers with three distinct microfabrication services: deposition (the addition of materials), lithography (the defining of materials), and etching (the removal of materials). Cutting-edge processes and equipment include a high-temperature furnace, low-pressure chemical vapor deposition (LPCVD), E-beam evaporator, sputtering, photolithography, isotropic wet or dry etching, anisotropic wet or dry etching, and metal lift-off.

Some of Wayne State's faculty members are utilizing the lab for projects that include retinal processors that cause less tissue irritation and more comfortable wearable health-monitoring devices, balloon catheters, and stents; environmental sensors for preventing invasive species in the Great Lakes; a chronic neural prosthesis using high-capacity graphene electrodes and biodegradable silicon support to treat a variety of neurological illnesses; the development of micro-electrochemical electrodes for neurological research that may have significant implications for those battling

depression and other mental disorders and the investigation the correlation of transport properties with edge structure in suspended graphene nanoribbon field effect transistors, which could have possible applications in touch screens, solar cells, fast transistors, gas sensors, and lightweight, high-strength materials.

ILC Dover Receives Class 7 Cleanroom Certification

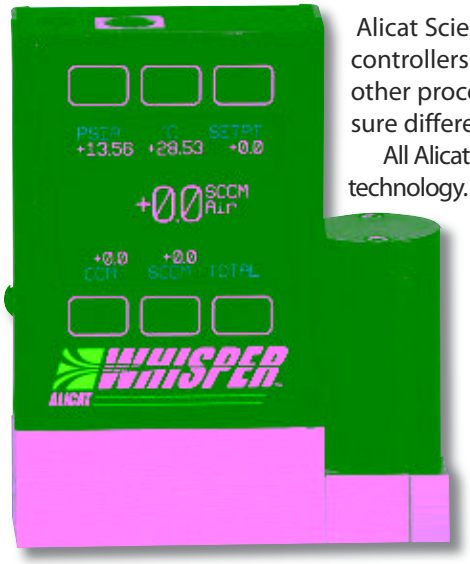
ILC Dover, the designer and manufacturer of NASA's space suits and a wide range of engineered film and fabric products, has received certification for its ISO Class 7 cleanroom. Testing of the cleanroom was performed in accordance with ISO Standard 14644 and IEST RP-CC006.3.

This facility will enhance ILC Dover's ability to support the global pharmaceutical industry with disposable systems engineered to contain powder transfers from cGMP to nanogram levels. These systems support cost effective manufacturing every day with applications ranging from single use transfers to multi-use flexible enclosures.

"The ISO Class 7 cleanroom will allow us to expand our powder transfer offerings and better serve our biopharm customers," says Chris Rombach, Biopharm Products Manager for ILC Dover. "ILC has a long history of supporting the powder containment and handling needs of the pharmaceutical industry and this added capability with further enhance our ability to deliver customer-focused, cost-effective solutions to the biopharmaceutical market."

The first product line to be produced in the newly certified cleanroom is the EZ BioPacT–a powder transfer system to support media and buffer preparation. Made from ArmorFlex, the EZ BioPacT is designed to reduce contamination that typically occurs during filling a powder transfer bag or, more importantly, when it is discharged to the reactor or mix tank.

Gas Meters and Controllers



Alicat Scientific's Whisper series of mass flow meters and controllers saves time and money in semiconductor and other process industries with systems using very low pressure differentials or exotic gases.

All Alicat meters and controllers are based on laminar flow technology. The Whisper Series achieves a differential pressure range of .01 to 2.0 PSID, depending on flow rate and configuration.

Whisper flow meters and controllers can operate as standalone devices or integrate into process control instrumentation. In addition to mass flow, a single device measures pressure, temperature, and volumetric flow. For applications requiring precision gas flow control, the device delivers flow regulation of gases with the ability to respond to upstream gas flow changes.

www.alicat.com

Air Amplifiers

Exair's Super Air Amplifiers have no moving parts, assuring maintenance-free operation. No electricity is required, and flow, vacuum, and velocity are easy to control. Outlet flows can be increased by opening the air gap. Supply air pressure can be regulated to decrease outlet flow. Both the vacuum and discharge ends of the air amplifier can be ducted, making them suitable for drawing fresh air from another location, or moving smoke and fumes away. Cycle time is reduced when aluminum casings are cooled with the high-volume airflow of two air amplifiers. The Super Air Amplifiers boost the amount of airflow throughout the air amplifier. Additional free air (room air) is pulled through the unit while delivering a more balanced flow, which is intended to make the Super Air Amplifiers run quietly. Force and flow can be adjusted using shims. Five sizes in aluminum are available.

www.exair.com

Gas Detector

The gas detector from Sensor Electronics is designed to protect areas where toxic/explosive gases, including hydrogen chloride and ammonia hydrides, pose a constant hazard.

The detector "sees" only one specific gas and cannot be confused by other gases that could cause false readings or alarms, or needless shutdowns. The stainless-steel construction repels corrosion, contamination, condensation, dust, dirt, aerosols, and temperature/humidity extremes. Factory-tuned for specific gases, the detector can turn on alarms to warn personnel. If gas concentrations increase, the detector can turn on fans to flood the area with outside air.

www.sensorelectronics.com

Pneumatic Metering Pump

The PPM100 pneumatic metering pump from White Knight Fluid Handling can dispense up to 100 mL of corrosive media with 0.1% repeatability at high-pressure (60 to 85 PSI). It offers adjustable flow rates for use in single-wafer processing tools or in premix vessels.

The pump is designed for chemical replenishing, blending, dosing, and spiking applications, as well as uses in cleaning of CVD equipment and photolithography. It is suitable for photoresist, etch and clean processes, peroxide spiking in piranha mixtures, and other blending of chemical mixtures into process tanks prior to the introduction of substrates.

www.wkfluidhandling.com

Slide Gate Valves

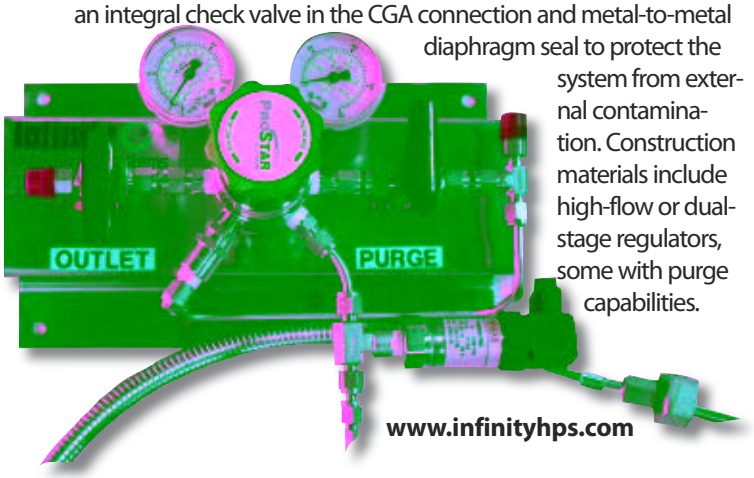
Mucon has developed a range of pneumatic and manually actuated double flanged In-Line Slide Gate Valves. The Mucon Slide Gate Valve's features include a shut-off solution that is suitable for powders, granules, and pellets. Its self-compensating polymer seal ensures that the blade is completely dust tight which prevents material leaking into the environment. It also offers total unobstructed full bore opening for smooth, non-jamming operation, and the unit is self-cleaning as well.

www.kemutecusa.com

Gas Delivery Panels

Infinity High Purity Systems offers standard gas delivery panels as well as custom designed panels to meet both installation and operation requirements. Options include one, two, three, or five valve panels for source panels, and a variety of multi gas centralization secondary point-of-use panels. The source panels also offer an optional ability to integrate real-time gas monitoring, as well as gas monitoring systems.

All gas delivery systems are affixed on a custom designed stainless steel panel, which is mountable anywhere or designed to fit, in order to maintain the reliability of the regulator and to provide ease of maintenance for all components. Every panel features an integral check valve in the CGA connection and metal-to-metal diaphragm seal to protect the system from external contamination. Construction materials include high-flow or dual-stage regulators, some with purge capabilities.

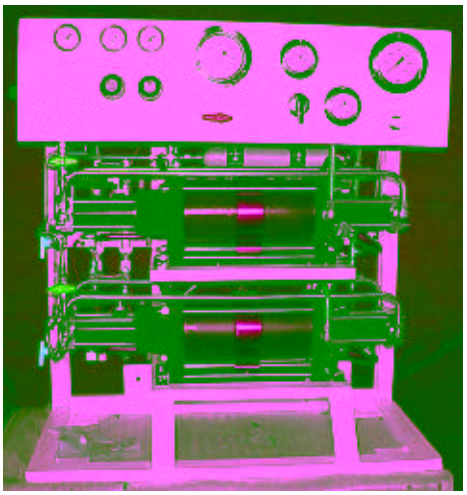


www.infinityhps.com

Pressure Boosting Systems

Va-Tran Systems Inc. manufactures a series of pressure boosting systems allowing the use of a low-pressure bulk CO_2 supply in applications where bottled CO_2 has been used in the past. These pressure boosters supply a Va-Tran liquefying CO_2 purification system under continuous duty driven by only compressed air. CO_2 cylinders no longer need to be moved about a facility and floor space is preserved in laboratories and workspaces.

A basic booster pump includes an automatic shut-off valve, relief valve, outlet filter, inlet air drive controls, and gauges mounted on a panel in an aluminum roll bar frame. The systems are customizable depending on need, and available add-ons include cycle counters, alarms, and status lights.



www.vatran.com

Air Quality Monitor

The AQ Expert indoor air quality monitor from E Instruments performs IAQ parameter testing to detect mold or other air-borne bacteria formed from outside pollutants.

The unit can run up to 11 parameters simultaneously, and provides real-time continuous data logging for graphs, data review, and IAQ reports. It provides wireless communications with Bluetooth, and includes PC software and USB. Other features include an active internal sampling pump, a li-ion rechargeable battery, a swivel handle, and an optional handheld probe and wireless remote printer.

www.e-inst.com

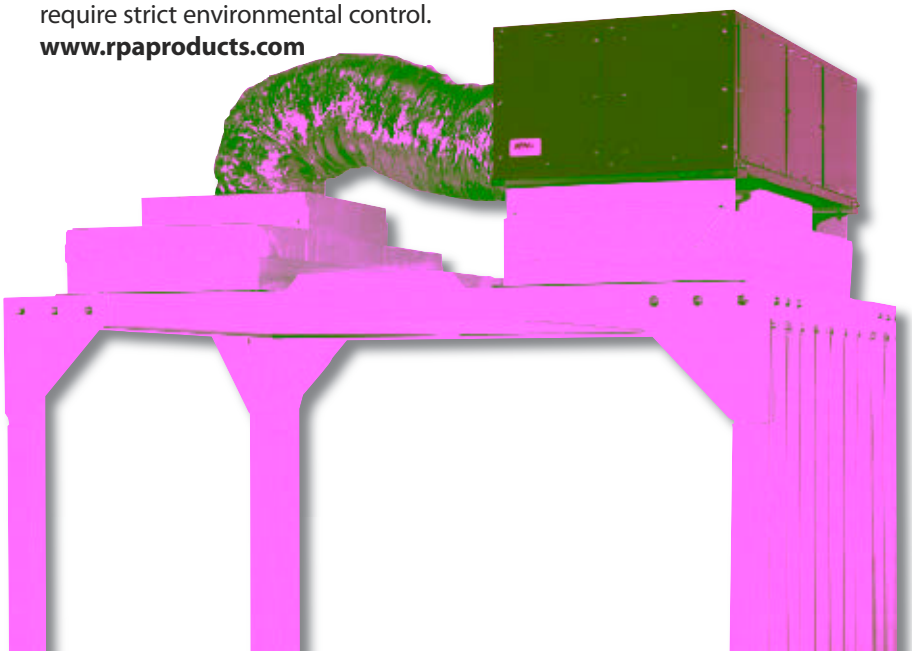
HVAC Module

RPA offers the HEPAir Integrated Modular Environmental System for modular cleanrooms, mini-environments, and process isolators.

This compact, self-contained HVAC module is designed to sit on top of a standard HEPA fan/filter module and deliver temperature- and humidity-controlled air to a controlled environment. One HEPAir can deliver air-conditioned air to up to three FFMs, and multiple units can be combined for control of larger cleanroom environments.

HEPAir and HEPAiRx products are produced by CleanroomSystems, a division of AiR INNOVATIONS, a provider of modular HVAC and ECU products for aerospace, semiconductor, and pharmaceutical industries that require strict environmental control.

www.rpaproducts.com



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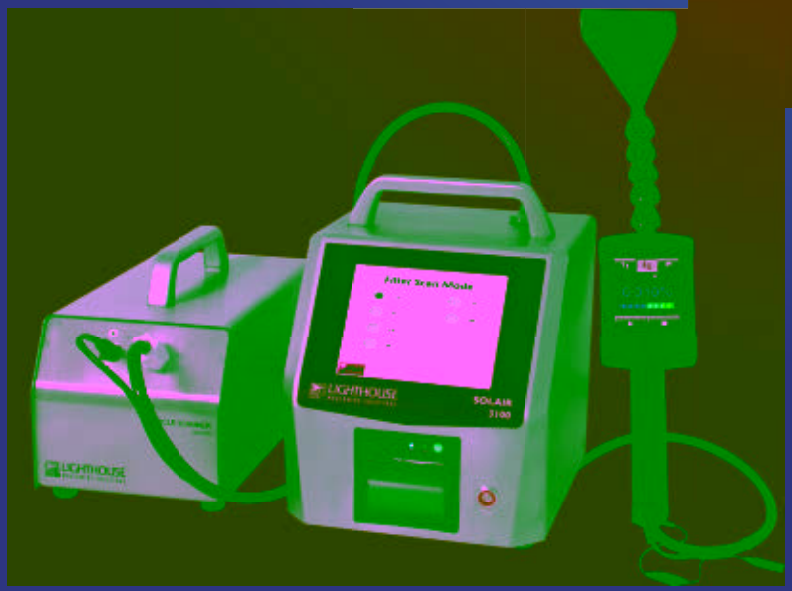

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