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Parenteral Packaging 2021: A Q&A with Conference Chairs

PDA Europe

[Editor's Note: The following is an interview conducted by PDA Europe staff with the Chairs of the 2021 PDA Parenteral Packaging Conference Planning Committee: **Roman Mathaes,** PhD, Lonza, and **Galen Shi,** PhD, Eli Lilly and Company.**]**

What are the major innovations and trends in the packaging eco system?
Primary packaging innovation has always been following and enabling trends in therapeutic modalities of pharmaceuticals.

For example, Cell & Gene therapy (CGT) is offering the treatment of life-threatening disease. However, CGTs feature a unique target product profile demanding innovation in container closure system solutions and associated analytical test methods.

Cold storage and supply chain of sterile container closure systems remains a significant challenge for container closure integrity. Oligonucleotide delivery requires a deeper understanding of the compatibility of molecule, formulation matrix and container closure system and delivery device.

The regulatory landscape regarding pharmaceutical packaging is evolving fast. The introduction of closed system transfer devices left the pharmaceutical industry with several challenges. Finally, the COVID-19 pandemic helped foster a dialog on high volume and rapid packaging development between governmental organizations, packaging suppliers and the pharmaceutical industry. On top of the technical challenges, it is important to pay attention to user interface and patient needs for improved patient experience.

Can you see a paradigm shift regarding packaging development and commercialization during the COVID-19 pandemic?
The COVID-19 pandemic brought some specific challenges to parenteral packaging suppliers and the pharmaceutical industry.

At first, the concern and discussion focused on the world manufacturing capacity of suitable primary packaging components for a potential COVID-19 vaccine. This concern could be invalidated by some packaging supplier even when considering a vaccination campaign of the world population. The dialogue shifted to *rapid* packaging development and a discussion on suitable container closures for potential vaccine or antibody treatments with a focus on speed to market, cost efficiency and supply chain challenges in certain areas of the world. The flexibility and agility of product development including parenteral packaging become utmost important to COVID-19 treatment, while maintaining the traditional requirements and quality and safety. We expect the legacy of enhanced speed and efficiency in parenteral product development will remain even after COVID-19 pandemic.

How do you see the PDA packaging conference evolving from 2020 to 2021? Can you elaborate on the Conference theme Parenteral Packaging in a New Era: Convergence of Patient, Process and Product Needs?
The PDA packaging conference continues its evolution to discuss packaging development holistically in a bigger context of combina-

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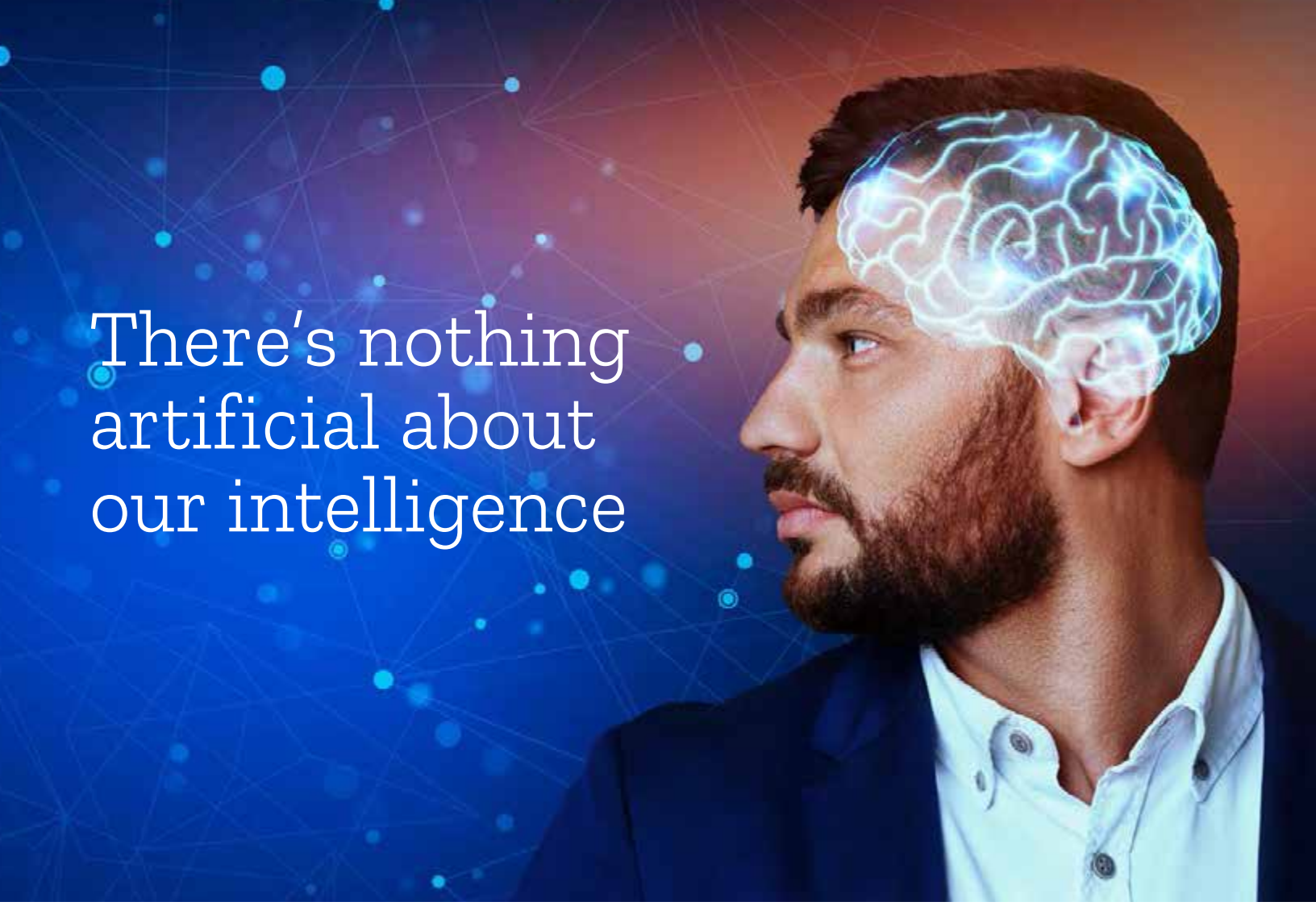

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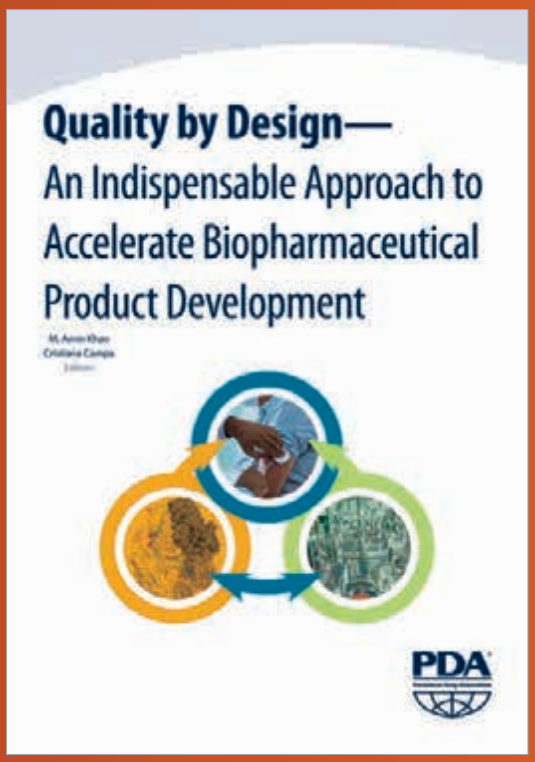

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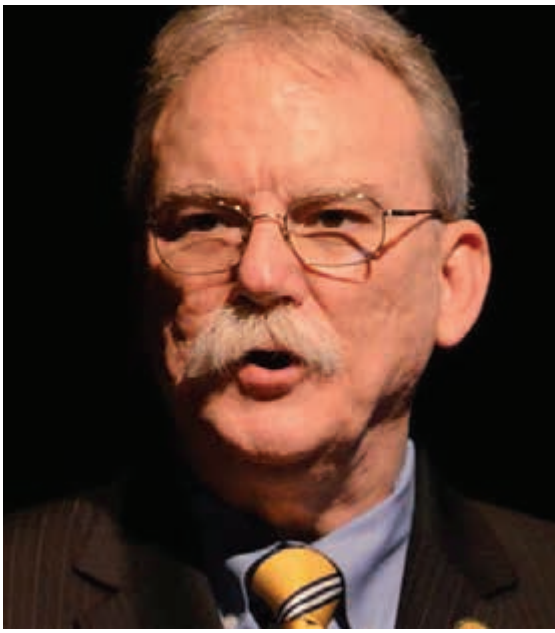

Richard Johnson, PDA

We finally saw the end of a year like no other—2020. The global coronavirus pandemic challenged each of us, including our organizations, governments, and families.

First and foremost, we should consider the impact this has had on so many lives around the world. The health impact has been staggering, and it is hard to envision that as of January 12, 2021 almost 2 million people have died, and more than 91 million have been infected. In addition to the terrible health impacts, the control measures that are continuing to be implemented have affected many more people's livelihood and social activity.

But 2020 also saw our industry respond to the crisis in dramatic ways: continuing to supply critical medical products; rapidly developing diagnostics and treatments; and developing vaccines in an unprecedented short time. All our members, in ways large and small, contributed to this effort.

Here at PDA, we have been similarly called upon to deal with this crisis. We rapidly shifted our staff to remote working. We rescheduled, canceled, and restructured to virtual, dozens of conferences, workshops, and training courses. Through it all, we have striven to maintain the support for you, our members. Through your efforts, we continued to bring valuable information and content to members and non-members worldwide.

In 2020 we hosted more than 100 events, from conferences and workshops to webinars and training courses. Our team worked hard to rapidly assess platforms and implement virtual events. Our science and regulatory efforts yielded our first ANSI standard, 12 other technical publications, and 9 regulatory comments. We published translation of several technical reports in Japanese, Chinese, and Spanish. We launched Europe and Asian editions of the PDA Letter.

As we look forward to 2021, we know that the pandemic situation continues to have a major impact. Nonetheless we expect an even busier year, with global conferences both virtual and hybrid. Our technical pipeline is full, with almost 20 technical documents on track to be completed in 2021. There will continue to be significant impact, but there is light at the end of this tunnel. We will continue *Connecting People, Science and Regulation®* with your help and support. Remember, this is your association. I look forward to hearing from you in the coming year. Happy New Year.

Be safe, be positive and be proud of your contributions. Thank you for all you do!

Best Regards, Mit freundlichen Grüßen, Meilleures salutations, Distinti saluti, Saludos cordials, よろし.

Jette Christensen, PhD, Novo Nordisk

What Does 2021 Have in Store for Us?

Jette Christensen (Novo Nordisk), Chair PDA Board of Directors

First and foremost, I wish you all a Happy New Year. I sincerely hope that 2021 will bring you happiness, good health, and harmony.

2020 was a very unusual year. The COVID-19 pandemic changed our world and our way of living. We had to isolate ourselves, wear face masks outside the classified areas and our homes, and learn to work in different ways. Whether we work for a pharmaceutical company, a vendor, academia, a regulatory agency, or as a consultant, we have all been impacted.

Even the PDA organization has been forced to find a new way of working. For sure, 2020 was a challenging year, but we gained many good learnings that we can use to benefit members.

Sudden Move to Virtual Events

Last year, our Annual Meeting was the first meeting/conference that we had to change into a virtual event. Since then, we have held several virtual meetings and continuously improved the digital setup. The PDA staff has worked very hard on improving the quality of our digital solutions, and we are now in a position where we can proudly say that we provide participants with very high-quality virtual conferences and training sessions. We will, of course, still focus on refining and delivering the best possible virtual conference and training setups.

Event Calendar 2021: Virtual and Hybrid

For your kind information, we will continue our signature conferences--the Annual Meeting, Quality and Regulation Conference, PDA/FDA Joint Regulatory Conference, Pharmaceutical Microbiology Conference, and Universe of Pre-Filled Syringes and Injection Devices Conference. Conferences on new topics will be held, too, like the Robotics and Automation Conference.

We now expect that traveling across borders will remain restricted, at least during the first half of 2021, so our conferences will continue to be run solely on a virtual platform. When it traveling is safe again, we will offer both face-to-face and virtual events, often in a hybrid shape of the two. 2020 has shown us that virtual meetings provide some benefits, for example, that you do not need to travel and that our virtual conferences allow you the opportunity to watch the recorded video presentations when it fits into your time zone. However, we are painfully aware that you miss meeting face to face, networking and building new relationships, shaking hands, or sometimes even giving each other a hug.

COVID-19 Task Force

In 2020, our COVID-19 task force offered, among other things, a series of webinars on virology and coronaviruses, remote inspections, inspection preparation, FDA guidance on COVID-19, and modular manufacturing to enhance/upscale capacity.

In 2021, the task force will provide you with more valuable information on how to handle the pandemic in the pharmaceutical world. Please remember to check our website in order not to miss any important webinars.

[Editor's Note: Read Jette's full message here**.]**

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Another layer of PDA leadership resides at the grassroots level in the Chapter organizations. Regional PDA Chapters provide local services to the membership, including translations of PDA publications, networking social events, student scholarship and annual regulatory and technical conferences. Each Chapter is managed by volunteer leaders.

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Board of Directors Nominations Needed

The PDA Nominating Committee is seeking recommendations from members for candidates to fill Board of Director positions for terms beginning in 2022. Nominees must be current PDA members in good standing. Recommendations will be considered and evaluated by the PDA Nominating Committee and approved by the Board of Directors. This year's committee is chaired by Immediate Past Board of Director's Chair **Rebecca Devine** and includes current Board of Director's Chair **Jette Christensen** and Board of Director's Chair- Elect **Susan Schniepp**.

If you are interested in being considered or want to recommend a colleague, send the recommendation via email (nominate@pda.org) or mail to PDA Global Headquarters, Bethesda Towers, Suite 600, 4350 East West Highway, Bethesda, MD 20814, USA, attention: President. In addition to your recommendation, please include any other supporting information that may make it easier for the Nominating Committee to evaluate your recommendation.

Nominations are due May 10.

If you have any questions or feedback about the nominating process, please feel free to contact PDA President **Richard Johnson** (johnson@pda.org).

Parenteral Packaging 2021: A Q&A with Conference Chairs continued from page 1

tion product, therapeutic environment, healthcare, and social responsibilities. In the past, packaging development was an isolated, silo activity within a pharmaceutical company, while nowadays packaging development has become a fully integrated part into pharmaceutical formulation development, analytical development, and manufacturing. All development activities have a focus on the patient, whether safety, efficacy, or experience. The 2021 theme is a natural evolution from the 2020 theme, "Interaction of Product, Package, and Process," to stress the focus on patient needs and unique challenges associated with the new era ushered in by COVID-19.

At the PDA packaging conference, we connect suppliers, academia, regulatory authorities, and pharmaceutical companies. We have a diverse panel of speakers and moderators enabling a cross-functional dialog to share and set future industry best practices.

What are the technical focus areas and how does the new delivery modality (Cell and Gene therapies) dictate new packaging innovation?

The PDA packaging conference 2021 will discuss all current trends and hot topics in the packaging ecosystem: primary packaging solutions for CGTs, regulatory trends such as closed system transfer devices and combination products, drug-container closure-device interface compatibility. Additionally, we have invited **Prof. Gustavo Barreto de Melo,** Federal University of São Paulo, and **Professor Buddy Rather,** University of Washington, to foster the exchange between academia and the pharmaceutical industry and their suppliers.

What is your understanding of a patient centric packaging development strategy?

Patient-centric product design covers the whole gamut from drug substance, drug product, primary container closure, delivery device, label and packaging, which collectively shape up the user interface and patient experience. In particular, parenteral packaging should enable positive patient experiences, whether through different form factors to allow patient friendly design of delivery devices or facilitate dosing convenience and flexibility.

What will be the delivery mode of the conference in the given COVID situation?

The PDA 2021 Parenteral Packaging Conference, 27-29 April, will be an online event allowing remote presentations and participation. The digital conference platform will provide a broad spectrum of possibilities including live Q&A sessions, industry exhibition, poster sessions and networking opportunities.

About the Experts

Roman Mathaes, PhD, Head of Pharmaceutical Services, Lonza Drug Product Services

Roman is Head of Pharmaceutical Services at Lonza DPS. In this role, he is responsible for primary packaging development and testing as well as device testing, tox and technical batch drug product manufacturing and the Lonza DPS lab automation group.

Before his assignment Roman, worked within the Roche/Genetech network Basel/San Francisco. Roman is a pharmacist by training and holds a PhD in pharmaceutical technology. Roman is a adjunct member of the Pharmaceutical Department University Basel and authored 30 research papers in the field of Biotech Drug Product Development.

Galen Shi, PhD, Leader of Autoinjector Systems Engineering, Eli Lilly and Company

Dr. Galen Shi has been with Eli Lilly and Company since 2004 and is currently the Leader of Autoinjector Systems Engineering. He is responsible for the design and integration of primary container closure systems and injection devices. Galen has over 23 years of experience in the biomedical and pharmaceutical fields. He held leadership roles (director and group leader) in a variety of areas including formulation development and process engineering for small and large molecule drugs. His current responsibilities include leading a team on system design and development of prefilled syringes and autoinjectors for delivery of bioproducts.

The Moldy Nightmare: Questions and Answers, Part 1

Ziva Abraham, Microlite, Inc.

[Editor's Note: The following questions were submitted during the Oct. 22 breakfast session, Mold Contamination and Remediation—The Moldy Nightmare, of the 2020 PDA Pharmaceutical Microbiology Conference. The speaker, Ziva Abraham, an industry-leading mycologist, drafted answers to the questions. Questions were lightly edited for readability, and the Q&A's were organized into four broad categories: Mold Control, Disinfectants, Mold Identification, and Specific Molds. The Q&A for the last two categories was published in Part 2**.]**

Mold Control

If a firm created a control plan specific to mold (a subset of the microbial control plan for the site), what unique controls would you expect to be implemented?

First, understand the type of product, its mode of administration, and the prevalence of infections via the mode of administration.

Second, identify the mold from all classes/grades to understand ingress and transport mechanisms for the mold.

Third, map out the biotic and abiotic factors. Biotic means the ingress path and abiotic means conditions in the cleanroom that will allow proliferation of the mold.

Fourth, adjust the disinfection and cleaning program based on mold type and predominance, and monitor the program effectiveness via trend analysis of mold recovered.

If you see low-level recovery (1 or 2 CFU) on an airlock gowning bench every three months or so, with no other recoveries in the airlock, would you suspect inadequate cleaning practices?

Low recovery in gowning areas is a common phenomenon, as this is the entry point into the controlled areas from the uncontrolled areas. Having said that, it is important to have a science-based cleaning program to address all mold that can be tracked through foot-borne traffic. The cleaning and disinfection program should include use of a general-purpose disinfectant with a surfactant that helps break surface tension and aids in cleaning as well as periodic use of a sporicidal agent to address bacterial and fungal spores.

it is allowing it to stay in the air for longer periods of time.

Would you recommend that a firm create separate alert/action levels for mold, different from bacterial levels?

As mold does not have an infective dose like bacteria and infects by anchoring instead of endo or exotoxin production, it is beneficial to know the mold present in the cleanroom. More importantly, it is crucial to know if it is present proximal to open product. Setting alert and action limits may be beneficial, however, trending mold types recovered from all cleanroom classes/grades provides a better tool for understanding the mold type, its ingress path, and the effectiveness of the cleaning and disinfection program, as well as the possibility of the mold entering the product and causing harm to the patient. Often alert level excursions do not get much attention; thus, the risk may be missed.

If mold is found only in air sampling (not on surface), what should be the action plan?

Mold recovery in air samples may be due to multiple reasons. Surface contaminants can become airborne, so the source could be foot- or wheel-borne contamination brought in. Inadequate storage of monitoring equipment and inadequate wipe-down procedures can be another reason. Monitoring equipment without a HEPA-filtered exhaust is known to be a contamination source. Growth of mold in walls after leaks, compromised HEPA filters, or mold growing on seals can cause airborne mold recovery. It is also important to track the mold to its source and map the transport into the area where it was recovered. Often dead spaces (e.g., in cleanrooms where the air is not cleared due to the location of HEPA filters), returns, and cleanroom and barrier system integration may allow the contaminants to linger for a long time.

If the mold is found in filling areas, especially RABs, the area between the HEPAs without a diffuser membrane is hard to clean and can hold contaminants that can become airborne.

Finally, depending upon the mold species recovered, especially the deuteromycotous fungi, which proliferate very fast, an abi-

otic factor such as moisture, carbon source, mineral oil, etc., should be looked at.

In summary, the investigation should be based on the genus recovered and the source, and the remedial action should be based on the above-mentioned points.

Once the source has been determined, increasing use of sporicidal agent, especially where the mold source is found, and trending monitoring data to assess the effectiveness of remedial measures is recommended. If a decision for using fogging is made, as the root cause is undetermined, the chemistry of the fog, the fog size, and the number of foggers to be used to cover the area in question should be considered. The smaller the fog particle size, the more buoyant.

What are good preventative actions aging facilities can take to prevent mold?
For aging facilities, monitoring and trending provide valuable insight as to the health of the facility. Trending microorganisms provides insight into contamination types and sources. For example, leaks happen, surfaces become compromised. Once a leak happens, the building materials and moisture create an excellent breeding ground for mold. This mold stays dormant until the next leak. There have been facilities that have mold infested walls, and mold contamination is transferred from one room to the walls of other adjacent rooms over time. Baseboards, if compromised, allow moisture to seep into the foundation, which has ample mold. Mold, being motile, can then start growing into the wall and flooring materials.

A routine audit for compromised structures, HEPA filters, seals, doors, etc., can help in incremental upgrades to the facility while keeping contamination under check.

Disinfectants

What mold genus should be included in disinfection efficacy studies?
It is beneficial to use a USP-recommended *Aspergillus* strain along with the one or two predominant mold isolates recovered from the environment or product testing. Per the recent European standard, EN 13697, it is recommended to use the mature *Aspergillus* spores for disinfectant qualification.

Why do some molds fail during disinfectant qualification studies?
Disinfectant label claim testing is performed using colorless deuteromycotous fungi *Aspergillus* and *Trichophyton*. Disinfectants with fungicidal claims, while using this testing method, may not be able to kill some colored Deuteromycota, most Ascomycota, and some Zygomycota.

It is recommended to understand the structures of the mold recovered in the cleanroom against those tested for fungicidal label claim. In some cases, increasing the contact time may help with the required kill, while in other cases prevention is the best strategy.

Is rotation of cleaning agent essential? Is it true that microbes grow resistant to the cleaning agent?
There is no documented evidence of resistance, but to address all types of bacterial and mold contamination a rotation program utilizing a general-purpose disinfectant with surfactant, as well as a sporicidal agent, is effective at eliminating vegetative forms and spores.

Do you recommend a routine rotation of a sporicide? Or whether, by exception, is it sufficient if we are not finding any systemic mold issue.
Using a sporicide with reasonable frequency is a good practice. Mold is mainly brought into the gowning room via foot- and wheel-borne traffic. If tacky mats are not used and changed adequately, the mold may also become airborne. The mold can subsequently be transported to more controlled areas via personnel.

Use of sporicidal agent helps reduce mold from being tracked into the controlled environment.

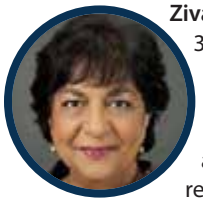
Can you comment on the degree of disinfectant resistance between fungi and bacterial spores?
Among the bacteria, the spore formers are harder to eliminate. For example, *Bacillus cereus* has the least kill even with sporicidal agents. It is hard for the disinfectant to penetrate the spore structure. As for ascomycotous mold, whose sexual spores are protected by two layers as compared to one layer in bacterial spores, it is harder to eliminate these fungi. Hence, preventing the entry of hard-to-kill bacterial spores and ascomycotous fungi that are soil or cellulous material-borne respectively is a winning strategy.

How do you recommend we clean or remove the residue from all of the cleaning agents on cleanroom surfaces?
Residue may be removed using quality water or residue strippers available on the market. Phenolic and quaternary ammonium compounds form most residues; hence the frequency of residue removal should depend on the use of residue-forming compounds.

Do disinfectants make claims against the sexual stages of mold? Are they tested against this?
For fungicidal label claim, disinfectants are tested against *Trichophyton* and *Aspergillus,* which are both colorless deuteromycotous fungi. This testing is performed per AOAC methods in the U.S. and per EN methods in the EU for fungicidal label claim testing.

These tests do not require testing with colored deuteromycota, ascomycota, or zygomycota.

About the Author



Ziva Abraham has over 35 years of academic, research, clinical, and industrial experience in microbiology and quality assurance. Abraham received her master's degree in microbiology with a focus on Mycology and has conducted research on developing microbial insecticides using entomogenous bacteria and fungi towards her PhD degree. She has also founded and managed clinical laboratories for Maccabi Medical in Israel. Abraham uses her extensive experience to teach why assessing the risk of microbial contamination should be in the forefront of any company that has products for human or veterinary use. Her experience in clinical laboratories has provided her with the framework to understand the effects of microbial contamination in products from a patient-safety perspective. Abraham is also the founder and CEO of Microrite, Inc., a California-based consulting and training firm with a focus on microbial and particulate contamination control