Connecting Pharmaceutical Knowledge

Great Lakes Chapter

Spring 2024 Newsletter

President's Message

Chris Timmerman
CAI | Client Manager

ISPE GL Chapter President

Hello and welcome ISPE Great Lakes Chapter members. I hope all of you had a great winter so far and spent some quality time with your families over the holidays. In case you missed the ISPE GAMP Forum in Chicago on January 25th and the Illumina tour and presentation of February 1st. We are planning to have more events throughout the chapter this year. Don't miss out on a great event and the opportunity to learn from industry experts and network with colleagues. Information will be out soon on registering for the upcoming events.

Student Chapters are the future of our industry. The Chapter is engaging with several of the Student Chapters that have been around for a while as well as working to establish a few new ones. Engaging people early in their career path is a great way to attract new members and new ideas that will benefit the industry. We also are heavily engaged with the Women in Pharma at the national level.

If you or anyone you know are interested in joining and helping us advance the goals of the Chapter, please reach out to one of the Chapter Directors. If you have ideas for topics that would be interesting and beneficial for the Chapter membership, we want to hear from you. If you have a particular location in mind for an event, please share those with the GLC Board. We want to hear what you have to say.

I, along with the entire GLC Board, appreciate all your contributions toward the Chapter's goals, bringing pharmaceutical engineering professionals together and providing learning opportunities for everyone. Please contact me at: chris.timmerman@cagents.com if you have something to contribute or would like to be more involved.

Member Spotlight: Keith Dodson

Keith Dodson —
Executive Director Business Development, Drug Product
Porton Pharma Solutions Ltd.

Tell us about yourself - how did you become interested in the pharmaceutical industry?

My journey into the pharmaceutical industry started when I was a co-op student at the University of Michigan studying mechanical engineering. I had the opportunity to work at 3M's heart & lung blood oxygenator manufacturing plant on process optimization. During the testing, you could feel the simulated 'pulse' of the heart/lung machine which made me realize that I was working on something which directly would keep a person alive. This moving experience caused me to focus all my future interest into the life sciences, landing a full-time position at 3M in their former pharmaceutical division.

Tell us what motivates you and drives your passion for the pharmaceutical industry?

I have worked in the pharmaceutical space for about 30 years now. Being on the leading edge of life changing medicine research and to work on supporting the eventual commercialization of successful molecules is a truly amazing experience. Having early glimpses into what treatments may be available in the coming 5-7 years gives me hope for conditions like dementia, diabetes, and severe depression which have impacted people close to me.

Tell us how long you've been a member of ISPE and what you've gained from ISPE and chapter membership?

I have been a member of ISPE for about 3 years now (joining late in my career). As a board member of the Great Lakes Chapter, I view this as an opportunity to both give back to the industry that has given me such a great career path as well as to continue to network with peers across the industry.

Is there something you'd still like to accomplish professionally or personally with the Chapter that our readers can help you with?

My goal is to continue to be part of ISPE and help guide our industry to solve the problems and challenges that we continue to face in our never-ending pursuit of better products, higher quality, and faster deliver of solutions to patients. I enjoy the opportunity to be a mentor to our young scientists, engineers, and professionals to help them make the most of their own careers.

Give us a little personal info – what you like to do outside of studies, family, where you grew up, etc.

Having grown up in the Midwest all my life, after working for several years across the country, I currently live outside of Chicago with my wife and children. My hobbies include music (singing and piano) and a love of all things in aviation. My family enjoys travel both within the United States and visiting as many international locations as we can.

2023 Great Lake Chapter Board of Directors:

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Technical Article

Sterilization Wrapping Evaluation for Compliance with EU Annex 1

Authors: Aaron Mertens, Renee Buthe

Introduction

European Union Good Manufacturing Practice Annex 1[1] requires pharmaceutical manufacturers producing sterile drug products to implement a Contamination Control Strategy (CCS) to minimize risk of contamination in their manufacturing processes. One source of contamination is materials entering the cleanroom area. The selection and evaluation of these materials is critical as expressed in EU GMPs Annex 1, Section 8.48:

> Where materials, equipment, components and ancillary items are sterilised in sealed packaging or containers, the packaging should be qualified for minimizing the risk of particulate, microbial, endotoxin/pyrogen or chemical contamination, and for compatibility with the selected sterilisation method. The packaging sealing process should be validated. The validation should consider the integrity of the sterile protective barrier system, the maximum hold time before sterilisation and the maximum shelf life assigned to the sterilised items. The integrity of the sterile protective barrier system for each of the sterilised items should be checked prior to use. (p. 27)

This article gives guidance for evaluating sterilization packaging materials specifically, as part of the CCS to ensure compliance with Annex 1. The following evaluation and rationale are the opinion of the authors and should be used as guidance in creating each manufacturer's individual CCS and associated risk assessment.

There are a variety of wrapping materials that can be used for in-process sterilization. In-process sterilization does not include processing of parenteral drug product or implantable medical devices. Sterilization wrapping constructed of spunbonded polyolefin material increases compliance when used for sterilization of direct and indirect product contact parts and equipment. There are many configurations and styles of sterilization wrapping to meet the unique requirements of the specific part that is being sterilized. For example, a flexible elasticized cover and drawstring sterilization bag is best suited for a stainless-steel stopper bowl, while a spunbonded polyolefin/film pouch is more appropriate for smaller items like tubing or forceps. This article breaks down the key requirements of Section 8.48 of Annex 1, and provides recommendations for evaluating sterilization wrapping compliance with the regulation.

Packaging Qualification to Minimize the Risk of Particulate Contamination

To minimize the risk of particulate contamination, sterilization packaging should be constructed of materials that contain low levels of surface particulate and shed minimal particulate during the wrapping and unwrapping process. Sterilization wrapping comprised of virgin spunbonded polyolefin material is cleaner than cellulose-based wrappings. Performance simulation testing[2] has been conducted comparing particles generated during normal use of a variety of sterilization packaging materials. Results showed opening spunbonded polyolefin/film sterilization pouches generates less than 1/10 the particulates compared to cellulose/film pouches. Simulation testing was also performed comparing cellulose wrapping with soft structure spunbonded polyolefin wrapping on a stopper bowl. During both the wrapping and unwrapping process, there were fewer than half of the particles generated. This testing was conducted within an ISO 5 area using an environmental particulate counter to enumerate 0.5µm and 5.0µm particulates generated when the wrapping/ unwrapping process was performed.

Packaging Qualification to Minimize the Risk of Microbial Contamination

To minimize the risk of microbial contamination, sterilization packaging should be evaluated for microbial barrier performance. This ensures the packaging adequately protects the critical materials contained within during transport and storage post sterilization processing. Spunbonded polyolefin provides a better microbial barrier than cellulose, as tested using ASTM method F-1608-GP1260[3]. The ASTM method is a filtration test using *Bacillus atrophaeus*, which demonstrates spunbonded polyolefin is greater than 99.99% effective at spore retention. The following table shows a comparison between cellulose and spunbonded polyolefin microbial barrier properties.

Microbial Barrier Test Results[4]

Sample Material	Log Reduction Value (LRV)	% Microbial Spores Retained
Spunbonded polyolefin nonwoven cover (rigid structure)	4.32	>99.99
Spunbonded polyolefin nonwoven cover (soft structure)	4.45	>99.99
BHD Blue Wrap	2.21	>99
Kraft Paper	2.11	>99

Packaging Qualification to Minimize the Risk of Endotoxin/Pyrogen Contamination

To minimize the risk of endotoxin/pyrogen contamination, sterilization packaging should be free from surface endotoxins/pyrogens. To meet this end, manufacture and conversion of the packaging should be conducted in controlled areas that are ISO certified to minimize the exposure to endotoxins/pyrogens. Additionally, the surface of the packaging could be evaluated using limulus amoebocyte lysate (LAL) assay[5]. Rigid and soft spunbonded polyolefin material has been tested, demonstrating undetectable levels of endotoxins/pyrogen levels recovered from the material surface. [8].

Packaging Qualification to Minimize the Risk of Chemical Contamination

To minimize the risk of chemical contamination, sterilization packaging should be free from surface additives and/or coatings (e.g., anti-static treatments), as there is risk that the coatings could leave a residue on the product contacting parts/equipment during autoclave sterilization. Polyolefin materials specifically designed for use as medical grade or for pharmaceutical applications should be used for sterilization packaging.

Validation of Packaging Sealing Process

Construction of the sterilization packaging should be done using a validated process, to ensure reproducibility of form, fit, and function. For example, the heat sealing equipment and process for polyolefin and combination polyolefin / film pouches and bags should be validated. Routine confirmation testing should also be conducted to demonstrate adequate and reproducible seal strength. Any seals made by the end-user should be confirmed as adequate for resulting seal strength. These details are explained in EN868-5 regulation and can be tested using ASTM method F88[6] using a tensile strength machine.

Heat sealer parameters included in the validation might include temperature, dwell time and air pressure. For different types of sealers and cycle parameters, end-users could use the starting points below for validation of their sealing process. It is the end-user responsibility to ensure the seal and package integrity of the wrapping at the end of the sterilization cycle to confirm the sterility of the parts.

Example Heat Sealing Parameters

	Sealing Parameters			
Type of Material	**Temperature**	**Dwell Time:**	**Cool Temperature:**	**Air Pressure:**
100% Spunbonded polyolefin	150-152°C	2.0 Seconds	110°C	80 psi
Spunbonded polyolefin/ PET Film	141-143°C	2.0 Seconds	110°C	80 psi
Spunbonded polyolefin/ HDPE Film	148-152°C	2.0 Seconds	110°C	80 psi

Integrity of the Sterile Protective Barrier System: Maximum Hold Time and Shelf Life

As stated in EU GMPs Annex 1, Section 8.48, "The validation should consider the integrity of the sterile protective barrier system, the maximum hold time before sterilisation and the maximum shelf life assigned to the sterilised items."

Sterilization wrapping should be tested and proven to maintain an integral and effective sterile barrier post sterilization processing, during transport and storage of the critical items contained within. Shelf-Life Studies of sterilized items must be supported by validation studies, including demonstration that the wrapping is an adequate microbial barrier to ensure the sterility of the part or equipment until the time of use. This could be in the form of sterile hold time studies[7], conducted using a variety of parts, wrapping configurations, and closure methods supporting 30-days shelf-life. This data provides confidence as a starting point for the end-user validation for their unique circumstance at their site.

This justification should be incorporated into the manufacturer's CCS to demonstrate compliance and robust sterility assurance of sterilized items based on control measures. Compliance with Annex 1 is the responsibility of the end-user. The data reported in this article was generated through simulation testing and each end-user should evaluate their own unique processes to provide adequate justification.

Conclusion

This article discussed:

- Requirements from Annex 1 around section 8.48 dealing with sterilization wrapping
- Best and cleanest material to use in aseptic areas involving sterilization
- Best practices to minimize particulates within aseptic cleanroom areas
- What materials will protect sterile parts post sterilization in terms of microbial barrier
- Endotoxin and pyrogen information that is needed for in process sterilization wrapping
- Ensuring the cleanest material is used so chemical contamination is not an issue during sterilization
- How to confirm seal strength and heat sealing parameters
- Sterile hold time studies using routine methods at a manufacturing site

STERIS Life Sciences offers Purefit™ sterilization wrapping, which has been thoroughly evaluated, tested, and found to be the highest quality material available today, ensuring the end-user is compliant with EU Annex 1.

Aaron Mertens has over 24 years of experience in pharmaceutical manufacturing, with expertise in cleaning, disinfection, sterilization and contamination control. He has held several positions within the pharmaceutical industry, with experience working at pharmaceutical manufacturing organizations representing quality assurance programs and working with global industry regulatory agencies. He holds a bachelor's degree in genetics. Currently he is a member of STERIS Life Sciences Technical Services Team and is a member of ISPE Great Lakes Chapter and the ISPE Sterile Product Processing Committee.

Renee Buthe has been a member of STERIS Life Sciences Contamination Control Solutions as Technical Services Specialist since October 2021. In this role, Renee has responsibility for providing global technical support primarily for Sterility Assurance (i.e. biological and chemical indicators) and Barrier Products (i.e. sterilization wrapping), application and validation. For 5 years, Renee has held positions within the Pharmaceutical Industry, specializing in environmental monitoring, sterility assurance, disinfection, sterilization and contamination control in parenteral drug manufacturing.

References

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2. STERIS "Particulate Contamination is a Concern for Critical Product Contact Surfaces." LS351EN 2022.
3. American Society for Testing and Materials. "Standard Test Method for Microbial Ranking of Porous Packing Materials (Exposure Chamber Method)." ASTM F-1608, 2021.
4. STERIS "Microbial Barrier Testing for Sterilization Wrapping Systems." Technical Tip 455-200-0001.
5. United States Pharmacopeia. USP 85. Endotoxin Testing using Limulus amebocyte lysate. LAL assay, 2017.
6. American Society for Testing and Materials. "Standard Test Method for Seal Strength of Flexible Barrier Materials." ASTM F88, 2021.
7. A3P *La Vague n°77 Gene Therapy.* "Maximizing Sterility Assurance: Sterile Hold Time Testing for Sterilized Items Used in Parenteral Drug Manufacturing." April 2023.
8. STERIS internal testing for endotoxins on Tyvek material. Method generation by the PACE Lab, St. Louis, MO. 2023.

ISPE GLC Welcomes New Members

The Great Lakes Chapter consists of members in the states of Michigan, Wisconsin, Illinois, Indiana, Ohio, and Kentucky. The Great Lakes Chapter of ISPE welcomes 87 new members since September 2023. Please welcome them to the organization and the pharmaceutical industry.

JAMES FELTZ, Eli Lilly & Co , Indianapolis, IN

Christopher Leber, Carmel, IN

Emily Niemi, RoviSys, Galesburg, MI

Melissa Fryer, Exergy LLC, North Syracuse, NY

Carmen Rodriguez Clinchard, Ultimate Solutions USA LLC, Granville, OH

Nate Schlueter, Northstar Medical Radioisotopes LLC, Monona, WI

Ravi Shah, Batavia, IL

Sophia Weitzel, Eli Lilly and Co, Indianapolis, IN

Ryan Power, Exact Medical Manufacturing, Lancaster, NY

Megan Cho, Alkermes, WILMINGTON, OH

Paul Barter, Salas O'Brien, Mountain City, TN

Gal Alon, Penn State University, Ambler, Pennsylvania

Ashley Kuttler, Siemens, Philadelphia, Pennsylvania

Nafisa Nawshin, SUNY-University At Buffalo, Buffalo, New York

Zeel Patel, IPS, Whitehall, Pennsylvania

Andriy Romanchuk, IPS, Bensalem, Pennsylvania

Maria Useche Franco, Eli Lilly and Company, Indianapolis, Indiana

Giulia Herszage Rocha, Eli Lilly and Co, Indianapolis, IN

Casey Gooden, Brentwood, TN

Scott Martin, Carmel, IN

Guillermo Roman, Purdue University, West Lafayette, IN

Yiannis Kaznessis, AgThera, St. Paul, MN

Dennis Spurlock, Memmert USA, Eagle, WI

Mary Sturgeon, Lamar Johnson Collaborative, Chicago, IL

Akanksha Garg, , West Lafayette, IN

Steve Kreuzer, Illumina, Verona, WI

Adler Elliott-Rosenberger, Project Farma, Indianapolis, IN

Josh Dittmer, Olivet Nazarene University, Bourbonnais, IL

Jotham Drayton, Olivet Nazarene University, Bourbonnais, IL

Harris Hannah, Olivet Nazarene University, Bourbonnais, IL

Scott Leonard, Olivet Nazarene University, Bourbonnais, IL

Nathan Martin, Olivet Nazarene University, Chicago, IL

Noelle Miller, Olivet Nazarene University, Manhattan, IL

Cara Serpe, Olivet Nazarene University, Bourbonnais, IL

Marc Shuflit, Olivet Nazarene University, Bourbonnais, IL

Benjamin Taveres, Olivet Nazarene University, Monee, IL

Mark Wager, Eli Lilly and Company, Plainfield, IN

Richard Johnson, Hydrox Laboratories, Elgin, IL

Catherine Spengler, Thermo Fisher Scientific, Cheektowaga, NY

Yongmei HU, Maple Grove, MN

Abby Clegg, Findorff, Newport, KY

Tom Ganser, Findorff, Madison, WI

Menno Huiser, Findorff, Madison, WI

Ryan Jacobson, J.H. Findorff and Son Inc, Madison, WI

Caleb Johnson, Findorff, Janesville, WI

Hunter Muthig, Findorff, Newport, KY

Robbie Oldenburg, Findorff, Madison, WI

Pierre Rideau, J.H. Findorff & Son, Madison, WI

Barry Harnick, Eli Lilly And Company, Noblesville, IN

Jason Merryman, Kymanox, Kenosha, WI

Geoffrey Ong, ADVENT Engineering Services Inc., Chicago, IL

Wade Porter, JH Findorff, Madison, WI

Emilie Danca, Nippersink Consulting Group, Round Lake, IL

Jenna Gruter, Findorff, Sauk City, WI

Alan Rogers, Schneider Electric, Naperville, IL

Govind Sandhu, ELGA LabWater, WOODRIDGE, IL

Brian Green, The Austin Company, Portage, MI

Brian Reeves, The Austin Company, Portage, MI

Milena McFeeters, Refined Sciences, Madison, WI

Tony Hoch, Biodyne-USA, Fort Wayne, IN

George Condes, Burns & McDonnell, Chicago, IL

Aaron Schneider, Avantor Performance Materials, Barrington, IL

Randy Williams, Feldmeier Equipment Inc, Syracuse, NY

Tiffany Alponat-Gram, STERIS, Mentor, OH

Kai Swanson, Swanson Flo, West Bend, WI

Charlotte Frank, Nalco Company, Naperville, IL

Rohit Mankame, Mundelein, IL

Kitt Rupar, Golden, CO

Erin Geul, Xellia Pharmaceuticals, Bedford, OH

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Allison Kinsey, Madison, WI

Austin MacIntyre, Colgate, WI

Benjamin Long, Schoolcraft, MI

Alesha Kelly, University of Chicago, Chicago, IL

Muriel Campbell, Eli Lilly & Co, GREENFIELD, IN

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Mike Tragseiler, Hixson, Cincinnati, OH

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Zane DeBeck, CSL Behring, Bradley, IL

Anuj Srivastava, Beyondsoft, Hawthorn Woods, IL

Freddy Altomari, Blue Mountain Quality Resources, STATE COLLEGE, PA

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Tiago Pina, Krusinski Construction Company, Anapolis

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Access the most premier presentations offering compelling insights, strategies, and best practices from experts representing global health authorities and leading pharma organizations.

Volunteer Opportunities

Would you like to get involved with other professionals in the Pharmaceutical industry? Do you have a special skill or passion? Would you like to see new or different events to help you in your career? The Great Lakes Chapter of ISPE is looking for volunteers to help with organization of events in your area. If you are interested, reach out to the board members listed .

Technical Articles Wanted:

Do you have a technical discovery or best practices that you would like to share with the Pharmaceutical Industry? This is a great way to get recognized by your peers for the great work that you do every day. We are looking for technical articles for the Great Lakes Quarterly Newsletter>

If you have something you would like to contribute, please send to Amir Zandnia, azandnia@gbateam.com

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[1]Content to be shared on LinkedIn must be approved by member of GLC board. Limited to post per month. Post will start with *SPONSORED CONTENT*.

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Networking Opportunities

Whether networking at face-to-face events or collaborating online, the value of ISPE is in the links forged between industry professionals with common work challenges, connecting professionals and companies to practical guidance and dialogue between industry and global regulators.

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