ABSTRACTS

KEYNOTES

New Developments in Cleanroom Design (ISO 14644-4 rev.)

Frans W. Saurwalt, Kropman, the Netherlands

The current version of ISO 14644-4 dates back to 2001. Within ISO Technical Committee (TC) 209 working group (WG) 4 has been assigned the task to review and update this part of the 14644 and 14698 set of standards.

With the Committee Draft internal ISO balloting of 14644-4 being passed with comments, an overview of the relevant developments and addressed topics of modern cleanroom design will be given and the highlights discussed. This presentation will not present the current content of the revised standard but will give information on the new developments that are considered and discussed. It will also link to the recent ISO 14644-16 on Energy Management as well as parallels to work within CEN TC156 WG18.

PHARMA

PHSS initiative in preparation of Clarity on GMP Guidance notes covering 20 specific GMP topics with MHRA review before publication.

James L. Drinkwater, Chairman of Pharmaceutical & Healthcare Sciences Society (PHSS) & Franz Ziel, UK

To provide more applied guidance on environmental control and monitoring the PHSS the PHSS Aseptic processing special interest group are preparing GMP supportive guidance (has a meeting on 7 June 2019 to discuss the guidance initiative of preparation of Clarity on GMP Guidance notes). There was a well-balanced discussion group that included: three ex-MHRA senior GMP inspectors, representation from major pharma industry (GSK, Pfizer Ireland and Belgium, Ely Lilly France & Italy, Filling machine, Barrier technology and environmental monitoring system manufacturers together with academics involved in GMP.

All sixteen proposed guidance note were overview reference; presentation on PHSS Initiative Clarity on GMP Guidance notes 2019, with more detailed discussion focused around four guidance notes:

- Clarity on GMP Guidance note no.1 Assurance of sterility in Aseptic manufacturing of contact product contact parts – New and Existing filling lines.
- Clarity on GMP Guidance note no.2 Rationale for Environmental Classification, Qualification, and Monitoring for Aseptic process filling applications with Barrier technology.
- Clarity on GMP Guidance note no.6 Risk assessment in setting EM Sample locations for monitoring during classification, qualification/ process simulations/ Media fills and during routine production operations.

This presentation reviews key concerns of 2019 meetings above notes and current developments and practices in PHSS Guidance.

Current topics in GMP and Inspection Findings in the Area of Sterile Manufacturing

Senior Phamaceutical Inspector, Mervi Saukkosaari, Department Manager, Finnish Medicines Agency (FIMEA), Finland

This presentation reviews current inspection trends and last updates to GMP guidelines development status of Good Manufacturing Practices (GMP).

Preparation of a Contamination Control Strategy as an Annex 1 Requirement and Preparation of an Aseptic Containment Strategy if Processing Sterile Toxic or Biologically Hazardous Products.

James L. Drinkwater, Chairman of Pharmaceutical & Healthcare Sciences Society (PHSS) & Franz Ziel, UK

Filling of toxic or biologically hazardous sterile products that cannot be terminally sterilised requires and Aseptic-Containment Strategy (ACS) that fits alongside a Contamination Control Strategy (Annex 1 GMP requirement).

The approach to Aseptic-Containment has to balance intrinsic contamination risks that may compromise sterile product quality/efficacy and patient health with measures that protect process operatives from hazardous product exposure that may put their health at risk.

This presentation reviews following subjects: 1) Overview of Aseptic-Containment strategy and alignment with a Contamination Control Strategy (CCS). Including containment levels, OEB bands and containment 'Pyramid'.2) Examples of Primary and Secondary containment boundaries. & 3) Points to consider in application of Aseptic-Containment through process and support steps including Filling line set-up, Filling operations, line clearance, Cleaning/decontamination, recovery from atypical events; product spills, glass breakage, barrier and barrier glove loss of integrity.

Regulatory Requirements and Expectations including a Review of the New GMP Annex 1

NN, Ecolab

This presentation will review Annex 1 EU GMP / FDA / PIC/s and USP<1072> requirements and guidance, including a review of the proposed NEW changes to Annex 1. The requirements and best practice for personnel training, documents and records, preparation and use of disinfectants, rotation, cleaning and EM, transfer disinfection and validation will be reviewed.

GMP Annex 1 : Selection Criteria of Protective Garments for cleanrooms and Controlled Environments

Steve Marnach, DuPont Personal Protection

The draft revision of GMP Annex 1 from December 2017 has defined special requirements to minimize risks of microbiological, particulate and pyrogenic contamination during the manufacturing of sterile products.

"Processes, equipment, facilities and manufacturing activities should be managed in accordance with QRM (Quality Risk Management) principles that provide a proactive means of identifying, scientifically evaluating and controlling potential risks to quality."

Cleanroom garments are the only barrier against contamination from people. For the future it will be essential to fully understand the risks to quality cleanroom garment systems can reduce or increase because they form an important part of an holistic contamination control strategy.

HOSPITAL

HUS Operating Room Ventilation and Air Conditioning Design Guide

Aleksanteri Setälä, HUS Kiinteistöt Oy, Finland

Currently there is no valid standard for operating room ventilation design in Finland. Because of this, the design solutions of operating rooms have been diverse across different construction projects. However European Committee for Standardization (CEN) is working on a European-wide standard draft "CEN/TC156 WG 18" which focuses on hospital air quality and ventilation design. The standard defines two acceptable cleanliness classes based on operational CFU concentration. The classes are CL-1 (Ultra Clean Air) which is intended for high-risk surgery and CL-2 (Clean Air).

Helsinki University Hospital (HUS) is the biggest health care provider and second largest employer in Finland. It consists of five hospital areas: Helsinki University, Hyvinkää, Lohja, Porvoo and Västra Nyland.

While waiting for the standard HUS has composed a design guide which concentrates specially on operation room ventilation. "Operating Room Ventilation and Air Conditioning Design Guide" is based on the upcoming standard but also enforces/promotes other HUS-applied practices. The purpose of this guide is to ensure that the ventilation of future operating rooms is implemented in a way that has been proven to work and is in accordance with class CL-1. In addition, the goal is to streamline the design process as design practices are defined in the guide and do not need to be reinvented for every project. The guide – as well as the standard – affects not only designer but contractor too as it defines, among other things, all mandatory tests that must be performed before an operating room can be introduced.

Practical Safety Ventilation in Ultraclean Air Operating Rooms

Pedro Gandra, Considero, Sweden

When planning new ultraclean air operating rooms, often the first question is which is the preferred room air distribution system and what system is the best to meet the requirements of microbiological air cleanliness. Today, in Sweden, the requirement is a target level of 5 CFU/m^3 during the design phase, in order to ensure that the level of≤10 CFU/m^3 during infection prone surgery is maintained. This study is based mainly on the analysis of published scientific reports and other documentation. The focus is to compare the main principles for room air distribution systems, mixing and displacement principle and to see whether the requirements of microbiological air cleanliness can be fulfilled during ongoing surgery. Three different distribution systems available in Sweden have been compared. The room air distribution systems studied are: Mixing airflow/partly displacement, Unidirectional airflow (UDF) and "Temperature controlled airflow (TAF)" - A specific Swedish room air distribution system.

The result of the comparison shows that in operating rooms for infection prone surgery all three studied room air distribution systems could achieve the target level of 5 CFU/m^3 when the air volume flows are above 2 m^3/s provided that the total microbiological source strength does not exceed 10 CFU/s. The total microbiological source strength depends upon the number of people in the operating room, their chosen surgical clothing system, and their activity level.

Prefabricated operating rooms

Kari Solem Aune, Kowi, Norway

When applying for a new operating room, the customer should consider whether to construct it on site or apply for a prefabricated one. This decision will have huge influence on the further process and should be done in a very early stage. When decided, the decision needs to be developed, and the wanted interfaces must be recognized and described.

The number of possible suppliers for prefabricated operating rooms is increasing, and each one of them comes from different sectors. Some of them have their main experience from the building elements (walls, doors etc) or ventilation/technique area, others from the medical equipment and even from the AV-perspective. All those have their strengths and weaknesses and may be combined in different ways.

In this session we will highlight the project process, some common interfaces and how to deal with them in your project. What should be decided – and when? What are the benefits and disadvantages be choosing the one solution instead of the other?

Contamination risks evaluated with the LR-Method in unidirectional airflow at different air velocities

Bengt Ljungqvist & Berit Reinmüller, Chalmers University of Technology, Sweden, Johan Nordenadler, Karolinska University Hospital, Sweden

Operating rooms for patients undergoing infection prone surgery often have unidirectional flow supply air systems. Many systems installed in Europe have low air velocities, i.e. equal and below 0.3 m/s, while other supply air systems have velocities about 0.4 m/s. The purpose of this paper is to describe contamination risks in unidirectional airflow without obstacles at different air velocities.

Sterilization Department Topics would be Acceptable

Kari Solem Aune, Kowi, Norway

The sterilization department in a hospital is more or less a factory for producing sterile goods. This means, we need to understand the sterilizing process in order to design and construct the right solution for each hospital.

There are no common guidelines on European level yet, but based on the Swedish requirements and Norwegian experience we want to share our best practice. This session will focus on the sterilizing process as a basis for the demands, the project process and how to design and construct suitable rooms and ventilation system for this purpose.

Pass through Boxes Design and Performance Testing

Frans W. Saurwalt, Kropman, the Netherlands

Wherever cleanrooms are used, items need to be transferred into and out of the processing rooms. Although common in pharmaceutical facilities, especial autologous ATMP facilities do require extensive application of pass through boxes to provide transfer without the need for personal access. The design of pass through boxes can vary widely relative to the application. The EU GMP Annex 1 revision states it does not

recommend not active ventilated pass through boxes. Various forms of active, combined and passive ventilated types can be evaluated. As contamination control performance aspects are considered: flow/pressure cascade, order of magnitude of the cleanliness transition from less clean to cleaner or clean to less clean. For typical GMP / ATMP cleanroom situations various design studies, proof of concept tests and qualification tests of in actual projects are presented.

Hospital isolation room air flow patterns: CFD simulations

Hannu Koskela & Petri Kalliomäki, Turku University of Applied Sciences, Finland

Patients with airborne infectious diseases are placed to airborne infectious isolation rooms (AIIRs) in Hospitals. Hospital staff and visitors can be exposed to the airborne pathogens released by the patients when working/visiting in AIIRs. Staff and visitors protect themselves against airborne pathogens with personal protective equipment (PPE), like gloves, masks etc. However, PPEs might not always provide complete protection against airborne contaminants and hence supplementary cover is needed. Direct exposure to the patient released pathogens can be reduced by controlling the airflow pattern with air distribution or local ventilation solutions.

In this study, computational fluid dynamics (CFD) methods were used to study air flow patterns and HCW exposure to the patient exhaled air in an isolation room setup. CFD simulations are widely used in ventilation research and provides an efficient tool for characterizing the local airflow patterns and effectiveness of the ventilation solutions. Three different air distribution methods were investigated in this study: mixing, zonal and displacement ventilation. Unsteady RANS (URANS) was used as a computational method. In the simulations, HCW was standing next to a patient bed and the patient was lying on the bed. The patient and the HCW were breathing out through nostrils with a normal breathing cycle. The simulations were compared against experiments carried out in a full-scale isolation room model.

URANS predicted realistic flow patterns when compared to experimental smoke visualizations. Also, the HCW's exposure was relatively well estimated by the URANS method. Zonal mixing ventilation seemed to work most effectively in reducing HCW exposure. On the other hand, air velocities close to bed area were notable with the zonal ventilation and hence it might cause draught and thermal discomfort in long term usage.

CLEANROOM NEWS / GENERAL

New, Chemical Free and Automatic Disinfection Technique - Enhancing the Antimicrobial Effect of Blue Light

Camilla Höglund, LED Tailor, Finland

The antimicrobial effect of blue light has recently attracted a lot of attention as a new technique for disinfection of surfaces and air. Antibiotic and chemical resistance among microbes has been recognized as a global threat, encouraging the search for new methods to eliminate HAIs (Health-care associated infections).

A 12 month study conducted by a Medical Center in the US, has showed a 73% reduction in SSIs (surgical site infections) in one operating room during the following year after an automated blue light disinfection system was installed. This is the first long-term clinical study showing actual reduction in SSIs as a result of adding blue light photon disinfection to the disinfection procedures in the operating room.

Studies have shown blue light to be effective in inactivating a wide range of microbes; Gram-positive and Gram-negative bacteria, moulds and yeast. Blue light can penetrate biofilm and inactivates microbes regardless of their antibiotic resistance profile.

A photocatalytic coating can be applied to environmental surfaces to enhance the antimicrobic effect of blue light. In addition, the photocatalytic coating inactivates viruses, spores and VOCs effectively. A TiO2-based photocatalytic coating activated by low intensity blue light (0,7 mW/cm2) has been shown to drastically enhance the inactivation of Staphylococcus aureus on a table surface.

Blue light offers a chemical free, continuous disinfection of the air and surfaces. It is a modern technology, safe for humans and surfaces, and worth to consider as a complement to the existing disinfection systems.

Digital Twins: What is the value behind all the hype?

Francisco Forns-Samso, Granlund Oy, Finland

The Digital Twin concept is an emerging trend in the built environment. Essentially meaning the coupling of the physical system with its digital representation. The idea is that the digital information duplicates the information embedded in the physical systems and it is linked throughout its lifecycle. Digital twins are essentially used for simulation, monitoring, analytics and reporting. In practice, it is still unclear how digital twins create tangible value in the industry considering the complexity and diversity of buildings. It is logical to think that a building might have several digital twins that serve a specific function or purpose. The aim of the presentation is to show the untapped the benefits of digital twins beyond the hype with real case examples. In this presentation, we will show:

1) how digital twins can enables to integrate existing and new information for improved analysis and visualiztions;
2) how we can reuse existing information for supporting different use cases;
3) how the integration of information enables the creation of new information to better understand the building behavior and improve decision-making process.

Microbial risk assessment with the LR-Method in safety cabinets/Class II benches

Bengt Ljungqvist & Berit Reinmüller, Chalmers University of Technology, Sweden

Microbiological risk assessment with the method for limitation of risks, the LR-Method, is described in this paper. Results from excerpts of case studies in safety cabinets/Class II benches are discussed. The LR-Method, which relies upon visualization of air movements, particle challenge testing, and calculation of a risk factor, presents an effective way for limitation of potential microbial airborne risks.