

ABSTRACTS 2009

OPENING PRESENTATION

A0 The crime of the 21ST Century counterfeit medicines

Gerry Prout, Kennet Bioservices Limited, UK

Counterfeit medicines are medicines that are "deliberately and fraudulently mislabelled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products. Counterfeit products may include products with the correct ingredients or with incorrect ingredients, without active ingredients, with insufficient active ingredients, or with fake packaging." (WHO).

Counterfeit medicines can harm patients in a number of ways and have caused deaths in a number of countries, particularly in Africa and South East Asia.

Improper treatment is a risk to public health in several ways.

If counterfeit medicines can get into the legitimate supply chain, the reputation and credibility of national and international healthcare systems can be adversely affected. Global sales of counterfeit medicines may reach USD 75 billion by 2010.

In 2006 WHO created the global partnership International Medicinal Product Anti-Counterfeiting Taskforce (IMPACT). All 193 WHO Member States are involved via national agencies, customs and police organizations, pharmaceutical manufacturers and wholesalers associations and health professionals and patient groups.

Examples of counterfeiting and the consequences will be discussed.

PHARMACY AND BIOTECH

A1 Counterfeit Medicines a global issue

Tor Gråberg, Läkemedelsverket, Sweden

The area of counterfeit medicines is a global issue and creates a huge hazard to patients and companies.

The current legislation dealing with Good Manufacturing Practice (GMP) and how the regulatory bodies address the impact from counterfeit medicines will be discussed. What risks can we estimate and how can we handle the situation? The new initiative from European Commission will also be highlighted. This legislative proposal aims at strengthening EU legislation to better protect EU citizens from the serious threats posed by fake medicines. The overall principle of the proposal adopted by the European Commission is to protect the legal distribution chain from the infiltration of fake medicines.

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A2 A story from the scenario to shut down pharmaceutical operations to a success story with Chinese ownership.

Anders Ulfhielm, Rechon Life Science, Sweden

The speech will cover a 5 year travel from the Executive decision to shut down the manufacturing site in Malmö to the foundation and operations of a new pharmaceutical company with Chinese ownership. Anders will guide you through the ups and downs during the different phases.

The presentation will also convey the experiences on how to collaborate with Chinese management and how to manage the culture differences.

A3 New Closed Vial Aseptic Filling Technology

Francoise Delhalle, Aseptic Technologies, Belgium

A new Closed Vial aseptic filling technology consisting in filling plastic vials by passing a needle through the stopper and then restoring closure integrity by laser sealing has been developed.

The new concepts of filling equipment and closed, clean, sterile and ready to use container have been fully validated.

The Validation Master Plan considers all the aspects of the technology, from the plastic materials, up to the full Process Qualification by Media Fill simulations. It includes the validation of the vial manufacturing process and the validation of the filling equipment.

Properties of the vials after filling, ageing studies and particular applications are also considered in the VMP.

A4 New developments in the field of Disposable Bioreactors for the Biopharmaceutical Industry:

Davy De Wilde, Sartorius Stedim Biotech, Belgium

Disposable bioreactors gain more and more importance in the biopharmaceutical industry. This technology doesn't only bring a significant cost saving by decreasing investment and operation cost, it also offers numerous other benefits such as reduction of contamination risk, easy handling and faster changeover between batches. This paper discusses the numerous advantages of this technology and describes a completely new type of disposable bioreactors. Its design is completely based on that of classical re-usable bioreactors. Thanks to this design transfer from re-usable to disposable has never been so easy. Not only does it offer the same flexibility in mixing, gassing and control as a classical bioreactor, the results which will be presented in this paper in terms of K_{La}, mixing times, cell viability and cell densities clearly show the impact that this bioreactor will have on modern cell cultivation.

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A5 Features, supervision and monitoring for a low throughput aseptic filling of potent product in isolator

Didier Meyer, Getinge, France

Vial filling of potent drug for clinical trial and hospital reconstitution of cytotoxic drug have to be done accordingly to the current Good Manufacturing Practice. The state of the art leads to use isolator technology as the best cross contamination barrier versus chemical and biological risks. The application of the Quality Risk Management from ICH Q9 gives the proper frame to this technology for identify, evaluate and control on a continuous basis the quality of such a process. This paper backed up with significant examples, shows the process in progress with its permanent qualitative and quantitative assessments.

A6 Designing of Personnel and Material Air Locks

Kurt Nordén, Biovitrum

Layout - The facilities shall be design to prevent mix-ups and cross contamination by minimizing crossed flows in the process. This includes flow of personnel, flows of clean and unclean material as well as sterile and non-sterile material. Consider product flow, flow of starting material and the need for communication. The facilities shall be design to minimize the movements for the personnel.

Air locks - Passage between areas of different grades shall be done through air locks. There shall be separate air locks for personnel and material. Air locks shall be fitted with systems that prohibit opening between different grades at the same time. When an air lock consists of more than one room, the two inner doors shall not be able to open simultaneously.

Personnel air locks and Material air locks - Personnel air locks shall consist of at least two rooms. Hand wash shall be performed in the first stage of the air lock. Wash basin taps shall be equipped with a photocell. Disposable towels of non shedding material shall be used. The final stage of the air lock shall fulfill the specification for airborne particles and microorganisms for the same grade into which it leads. To fulfill the specification the air lock shall be equipped with air supply. Material air locks should consist of at least two rooms. In- and outtake of material shall be separated either in room or time. Room differential air pressure gauges shall be installed and continually monitored by a surveillance system and alarmed.

A7 Designing a new filling plant with energy consumption in mind

Ulla Thomsen, NovoNordisk A/S, Denmark

2008 with soaring energy prices and 2009 which seems to promise new international commitments to climate savings both put new light on how energy is expended. This paper explores the process of designing a new pharmaceutical facility and the decisions made in order to reduce the amount of energy the plant will use when operating. Special focus will be on HVAC design.

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A8 Improved Quality Assurance When Integrity Testing Multiround Housings

Pascal Martin, Meril and Magnus Stering, Sartorius Stedim Biotech

A new approach for integrity testing was carried out at Meril France in Lyon for improving the quality assurance when integrity testing large sterile filter systems such as multi-round housings. The approach was defined after having compared the single point diffusion test and the bubble point test by means of a mathematical model using the test algorithms of the integrity test unit and integrating real multi-point diffusion test values from single filter elements.

The single point diffusion test will always reflect the overall diffusion rate of the cartridges being tested thus increasing the risk for a minor failure (e.g. one single non integer element) being potentially masked by the overall low diffusion values of the surrounding cartridges.

The bubble point will reflect the biggest pore sizes. Its' accuracy depends on the capacity of the integrity test unit to detect the over proportional increase when passing from the diffusive flow region to the bulk flow region. For a large filtration area this transition phase will be potentially masked due to the overall high diffusion rate.

The multipoint diffusion test will reflect the diffusive profile of the filter system over a broad range of differential pressures all the way up to the characteristic bulk flow of the bubble point thus integrating the advantages of the diffusion test and the bubble point test in one test.

The outcome of the trials was a customer specific multipoint diffusion test with high process security without being obliged to integrity test each filter element individually.

A9 Automated Sampling & Data Reporting of Microbial monitoring Contamination within the Pharmaceutical Industry

Thomas Lööf, Malvern, Sweden

Automated particle monitoring systems are explained, their design and their use in pharmaceutical industry today. Comparisons are made to the microbial monitoring. The regulatory recommendations are presented. Advantages and disadvantages of today's common equipment used for monitoring are commented. The question if microbial monitoring can be integrated into an existing or new particle monitoring system will be discussed.

Validation of automated microbial monitoring system will be discussed with regard to necessary documentation and adequate parameters to test.

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A10 Design of HVAC for Cleanrooms

Jörgen Pedersen, NNE Pharmaplan, Denmark

HVAC is just one small piece of a well working cleanroom - but a very important piece. Without a perfect HVAC system the desired conditions for production might not be achievable. HVAC-systems for cleanrooms are expensive and take up much space but they are essential for the product quality. HVAC-systems also represent large operating cost.

This presentation will focus on design considerations in connection with design of HVAC for cleanroom facilities in order to design the optimal HVAC-system with regards to function and economy. HVAC-systems may by nature vary very much from one part of the world to another due to traditions and local weather conditions - but when it comes to design for cleanrooms the conditions are very much the same no matter where you are.

The requirements for cleanrooms also are very much the same whether it's for pharmaceutical processes or operating theatres in hospitals

A11 How to use the risk analysis for determination of sample location for environmental monitoring in classified areas in a pharmaceutical company

Jette Christensen, Novo Nordisk A/S, Denmark

According to the new version of EU GMP Annex 1 paragraph 8, clean rooms and clean air devices should be routinely monitored in operation and monitoring locations based on a formal risk analysis study and results obtained during the classification of rooms and/or clean air device

This presentation will cover how to use the risk analysis for determination of sample locations for environmental monitoring of classified areas. The presentation will include a case study.

A12 Case Study: Qualification of a filling room and -zone.

Lene Blicher Olesen, Statens Serum Institut, Denmark

The study covers the performance of the qualification of a new filling room and - zone, and demonstrates the use of different cleanroom tests; recovery testing, flow studies, particle and microbiological monitoring.

C13 Cell Substrates. The Impact of Recent Technological Advances on Biopharmaceutical Product Safety and Regulatory review

Kathryn K. King, Biologist, Division of Monoclonal Antibodies, Office of Biotechnology Products, CDER, FDA

Scientific and technical advances within the biopharmaceutical industry over the past decade have given rise to novel issues that impact product safety and/or quality. The PDA cell substrate task force was established to examine how these

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advances affect upstream manufacturing of monoclonal antibody and therapeutic protein products produced in banked non-microbial cell lines. Using case studies as a basis, the task force is elucidating what approaches have been taken to address these safety/quality issues scientifically and with regard to current global regulatory guidelines. The topics encompassed by the task force range from the parental cell line through the testing of the unprocessed drug substance. This presentation will focus on three main areas of interest: 1) viral testing of cell banks and unprocessed drug substance 2) new cell lines and cell line engineering and 3) raw materials associated with cell substrates. The presentation will also address FDA's current perspective on ensuring the integrity and quality aspects of cell substrates.

C14 News from PDA

Speaker: To be announced

FOOD

B1 Microbial exposure assessment along the food chain

Pernilla Arinder, M.Sc , SIK, Sweden

Food should not contain microorganisms in quantities entailing an unacceptable risk to human health. When increasing food safety, one step to take is improving hazard analysis. Today, the main shortcomings of hazard analysis include difficulties estimating the extent and likelihood of the occurrence of a specific hazard along the production chain and quantifying the effects of control. This creates uncertainty with regard to correctly identifying hazards requiring control and the best means of their control. A substantial improvement of the microbial hazard analysis can be made by using quantitative microbial risk assessment. In the quantitative microbial risk assessment the increase of bacteria due to contamination, growth or concentration, respectively the decrease of bacteria due to inactivation or dilution is estimated taking into account the process and the product. This will enable more precise identification of the process, product and storage criteria, ensuring product safety in accordance with the requirements of the authorities and the customers.

B2 Tracing down the contamination source in food industry

Savvas Gennaris, Veterinary Services Cyprus, Cyprus

It is generally well known that the food industry is legally responsible for producing safe foods. On the basis of safe food production the aim is the design and manufacture of products with a good safety record. Nevertheless, breakdowns in the food safety/quality systems occur and lead to the presence

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of hazards within the food consumed. Major contamination sources are raw materials water, air, dust, equipment, sewage, insects, rodents, and employees.

The response in such cases must be immediate, efficient and be based on identifying the contamination sources in a structured way assuring the production of safe foods on one hand and decreasing or eradicating the hazard on the other hand.

This requires a multidisciplinary, step by step approach.

Reevaluation of the current situation; sampling and analyzing of raw materials, intermediate and final products, surface swabs, water and air are important steps of the approach.

Six pilot studies carried out in food producing companies in Cyprus suggest contamination sources that could pose severe risks for the product's safety.

B3 A practical approach to validate the risk assessment tool Hygram®

Satu Salo, Marja Vainionpää and Gun Wirtanen VTT, Finland

Own checking systems are created to maintain the quality of food products in processing. Estimation of the risks, their severity and probability, is based on experiences of the HACCP team led by the quality manager. The variation between estimations of risks made by various experts was studied in an exercise based on the Hygram® program. The process flow, other relevant background information on and data about levels of microbes measured in the fictive poultry ham factory was given to persons dealing with microbial quality of products and being either junior employers in food industry or young research scientists from new EU-countries. These persons were asked to estimate possible risks using the Hygram® program. The results of the evaluation performed showed that more attention must be paid to harmonize the risk assessment protocol. Furthermore, the expert leading the own checking needs to be experienced in order to understand the levels of possible risks.

B4 Pulsed electric field treatment for microbial decontamination

Maria Lövenklev, PhD, SIK, Sweden

Treatment by electric pulses has useful applications in biotechnology, medicine and also as a microbial decontamination technique. Pulsed Electric Field (PEF) is a non-thermal decontamination technique and is today recognised as a promising alternative method to heat treatment. In respect to food applications, one advantage with PEF treatment over heat preservation is that flavour compounds and nutrients are better preserved and therefore the possibility to develop safe food with fresh-like properties can be accomplished.

During PEF treatment, the bacteria are exposed to an electric field under short time resulting in membrane disruption and leakage of intracellular components.

Dependent on PEF treatment the exposed bacteria are killed

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or just injured; in the later case the induced pores in the cell membrane will reseal. During this time for recovery the bacteria are sensitive and stressed; a condition of the bacteria that can be used in combination with other decontamination and preservation techniques in order to achieve a relevant bacterial inactivation.

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C1 Air cleanliness in hospital: problems and solutions (Russian standard GOST R 52529)

Alexander Fedotov, Invar Project, Russia

Cleanrooms and clean zones in hospitals are in use for some 30-40 years. But there is still lack of systematic requirements for air cleanliness in hospitals in general. Sometimes there are contradictions between hygiene specialists and engineers. It is time to separate clearly responsibilities of hygiene and technical services. Russian standard GOST R 52529 "Air cleanliness in hospitals. General requirements" and results of testing cleanrooms in hospitals are discussed.

C2 Design of production sites for radiopharmaceutical preparations

V. V. Kanygin and V. D. Yakukhina, Russia

Manufacture of radioactive pharmaceutical preparations has several specific features and is different from other processes. The key features include the following:

- Combination of specific radiological requirements and GMP rules;
- Special equipment with protection from irradiation;
- Necessity to protect personal, environment and products
- Use special ventilation and drain systems;
- Specific measures to handle with radioactive wastes;
- Short shelf life (several hours and so on) isotopes requests special measures for quality assurance;

These features are to be considered during specification, design, installation, qualification and operation stages.

C3 Partikel- och bakteriemätningar i LAF ventilerad operationssal under implantatkirurgi

Carl Widmark, MD, PhD, Överläkare Anestesi-kliniken, Sjukhuset i Varberg

På sjukhuset i Varberg genomfördes den 28-29 oktober 2008 en undersökning av bakterie- och partikelhalten i luften i samband med ortopediska implantattingrepp. Föreningshalterna under uppdukning och operationens olika moment samt skillnad mellan föreningshalterna under

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LAF-ventilerat tak jämfört med övriga rummet kommer att presenteras.

Presentationen bygger på följande frågeställningar:

- Är det möjligt att duka upp under LAF-ventilerat tak parallellt med patientförberedelser utanför LAF-ventilerad zon utan att föroreningshalten under LAF-ventilerat tak påverkas?
- Hur påverkas föroreningshalterna av operationens olika moment?
- Påverkas renheten i rummet av antal passager genom dörrar i en utsträckning att man kan se en mätbar höjning av partiklar och CFU?

Sommaren 08 driftsatte vi en ny operationsbyggnad på sjukhuset i Varberg. Byggnaden är utrustad med sju stycken salar på 56 m² vardera och med ett i salarna asymmetriskt placerad LAF-ventilerat runt tak på 3,6 meter i diameter.

Operationssalarnas yta i kombination med LAF-ventilerat tak ger oss möjlighet att förbereda patient samtidigt som vi dukar upp på sal under kliniskt acceptabla förhållanden - sammantaget ger oss detta parallellprocesssystem logistiska fördelar inom den kliniska verksamheten.

C4 A new Department of Cellular Therapy, Norwegian Radium Hospital Cancer Clinic in Oslo

Merete Djupedal och Jan Holteng, Radiumhospitalet, Oslo

This presentation succeeds last year presentation in Denmark about a new Department of Cellular Therapy, Norwegian Radium Hospital Cancer Clinic in Oslo, Norway.

The 2008 presentation included a general introduction to the department, room and facilities layouts, the different classified areas and principles for logistics. That presentation also included how the validation process was planned and would be performed.

The 2009 presentation will focus on the project management and the close relationship and cooperation between the department and persons responsible for the operations and engaged consultants. It is not very often a new department is built. It is a challenge to establish a task force for every new project, identify the goals and limitations, activities, risks, costs and time progress. The EU - GMP validation process specify demands to involved management and staff and the process itself, including engaged consultants and suppliers.

In May 2009, the new department is assumed to have been operational for a couple of weeks. Can we confirm the projects success criteria, has the budget been exceeded and what about the time schedule? We will, based on our positive and negative experiences in this project, try to give specific advices to future projects.

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C5 Operationsrum med parallellströmning – En översikt

Bengt Ljungqvist och Johan Nordenadler, Installationsteknik, KTH

En översikt av parallellströmningssystem i operationsrum genomgås i denna presentation. Med utgångspunkt från Charnley's försök under 1960-talet redovisas utvecklingen i Sverige. Tekniska data som luftflöden, lufthastigheter och luftförling samt operationsrumskläders inverkan på halten bakteriebärande partiklar diskuteras.

C6 Operationsrum med parallellströmning – Resultatredovisning av ett licentiatarbete

Johan Nordenadler, Installationsteknik, KTH & Projektengagemang AB

Laboratorieprov enligt LR-metoden med partikelbelastning invid en person, som utfört relativt lugna armrörelser, visar att skyddsverkan i en parallellströmning påverkas av lufthastigheten. För att få en god skyddsverkan visar resultaten att parallellströmningens lufthastighet bör överskrida 0,4 m/s.

Dessa resultat har bekräftats med fältmätningar i tre olika operationsrum. Resultaten visar, då lufthastigheten är lägre än 0,3 m/s, att luftrörelserna ovan operationsbord blir oordnade och antar ett utseende liknande omblandande strömning. Om däremot lufthastigheten överstiger 0,4 m/s antar strömningsbilden en mer parallellströmningsliknande form. Då de flesta inblåsningssystem med parallellströmning, som installerats i Sverige de senaste 10 åren, har lufthastigheter lägre än 0,3 m/s blir strömningsformen ovan operationsbord omblandande. Fyra landsting har medverkat med data från pågående operationer, där halten bakteriebärande partiklar även har angivits. Med dessa data och resultat från egna mätningar har ett enkelt samband framtagits för att skatta halten luftburna bakteriebärande partiklar i operationsrum under pågående operationer. Detta samband, som bygger på utspädningsprincipen, visar relativt god överensstämmelse med registrerade mätvärden.

C7 Evaluation of clothing systems used in operating rooms

Berit Reinmuller, KTH

One common system of protective clothing systems commonly used in operating rooms have been evaluated in a test chamber (body-box used for evaluating cleanroom clothing systems) at Building Services Engineering, KTH. The results have been compared to results of clothing systems of higher and lower quality. Test results indicate that the level of airborne microbiological contamination from people in operating rooms is depending upon the filter efficacy of the selected clothing system.

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C8 State-of-the art Operating Theatre System with recirculated airflow as an important application of highend cleanroom technology*Alf-Edgar Geier, M. Sc., Vokes-Air Group Switzerland*

With the new Vokes – Air Group Operating Theater system, high protection of patients against life – threatening infections is fulfilled. Depending on the type of operation, the OP- system filters, cools and heats the air supplied via an extensive sterile type CG-screen air outlet. Simultaneously it produces a laminar (quasi turbulence-free) airflow.

Consequently creates an invisible separation of the OP-area from its surroundings and the penetration of bacterially or virally contaminated air can be effectively prevented by the use of Vokes- Air Group H14- HEPA filter technology. The concentration of germs present during the operation amounts to less than 10 CFU per m³ air below the sterile air outlet. Thus larger sterile air outlets mean the sterile OP-zone can be extended to cover the material and instrument deposit area and guarantees more comprehensive protection for the patient. Cost savings of up to 40 % on investment and running costs thanks to the minimization of the make up air volume and DC-blower technology become reality.

C9 CFU-mätningar i operationssalar med Sartorius-metoden*Magnus Johnsson, Scandfilter AB*

Postoperativa infektioner har alltid varit ett problem inom sjukvården, speciellt vid ortopediska operationer. Under de senaste åren har en mängd äldre operationssalar renoverats och utrustats med ny teknik och ny ventilation. Gamla operationssalar med omblandande eller deplacerande ventilation byggs om till salar med UDF (Unidirectional Airflow), populärt kallat LAF-ventilation (Laminar air flow), där man får lägre föroreningshalt i luften och därmed minskar risken för infektioner.

Scandfilter har sedan sju år tillbaka installerat LAF-tak för operationssalar. För att kvalitetssäkra funktionen och luftkvaliteten i operationsområdet har vi avslutat varje projekt med en CFU-mätning (Colonial Forming Units) enligt Sartorius-metoden. Detta har gett oss stor erfarenhet av mättekniken samt tillgång till mätdata från olika kliniker över hela Sverige. Resultaten pekar på väldigt låga värden av luftburna CFU.

Presentationen kommer att behandla följande punkter:

- Mätmetod för CFU-mätning (Sartoriusmetoden)
- Fördelar och nackdelar med Sartoriusmetoden samt alternativa mätmetoder
- Presentation av CFU-värden i operationsområdet från ett tjugotal olika LAF-taks-installationer.

I presentationen ges exempel från ett antal olika fall av industriellt renhetsarbete.

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C10 Prevention of postoperative infections - Hygienic measures and ventilation*Anna Hambraeus MD PhD*

By introducing antiseptic methods in the operating room Lister lowered the mortality after amputation from 40% to 15% during the years 1864 to 1866. The carbolic spray used attempting to kill airborne bacteria was soon abandoned as it had no impact on his results. By expanding Lister's techniques into the field of aseptic techniques postoperative infection rates were successfully lowered, e.g. Brewer lowered the infection rate after clean operations from 39% to 3.2% between 1895 and 1899.

In the UK the possibility of airborne bacteria as a risk in the operating room was brought into attention in the 1950s after investigations of reasons for high levels of *Staphylococcus aureus* surgical site infections. High counts of airborne bacteria and of *S. aureus* coincided with high infection rates. Not only ventilation needed improvement but also general hygienic measures. During the 1960s and 1970s the design of operating theatre suites were discussed and guidelines for prevention of surgical site infections were developed. These are by and large still valid today. During the 1970s adequate use of preoperative antibiotics further reduced the rate of surgical site infections.

An unresolved issue seems to be when to use ultra clean air and bacteria tight clothing in the operating room. There are several reasons for this e.g. infection rates in implant orthopedic surgery are very low, thus huge materials are needed to achieve statistically significant results for the effect of any hygienic measure, be it skin disinfection or ventilation, the relative importance of clean air depends on how effectively other routes of infection are prevented.

(Lecture will be held in English)

C11 Prevention of postoperative infections – infection control in commissioning and monitoring of operating theatre suites*Ulrika Ransjö, MD PhD*

The operating room is not a cleanroom – it contains many sources of micro-organisms, the most important of which is the patient himself. Therefore, the construction of the room cannot prevent all postoperative infections. Even so, infection control (IC) has an important role to play in the design of the operating room suite.

To design an operating suite, you need to consider flow in and out of the suite, not only of air and other gases but also of people – personnel and patients–, of medical products, of laundry and waste. Many actors are involved in the construction process, and basic principles for infection control are not always adhered to throughout that process. Architects, engineers, estate departments, medical staff, contractors and builders need to make use of the expertise available in IC departments for all the steps in the commissioning and monitoring of ope-

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rating theatre suites. In Sweden this is a legal requirement in order to guarantee patient safety. Some examples from Swedish hospitals will be given of when and how input from IC can affect the quality of care given in operating rooms. (Lecture will be held in English)

C12 To be Announced

BIOFILMS AND DISINFECTION

B5 Biofilms in the dialysis community

Helena Jeppson, Gambro, Sweden

Microorganisms attach to surfaces and aggregate in a bio-polymer matrix to form biofilms. Microorganisms growing in biofilms have different properties compared to their free floating counterparts. Biofilms are ubiquitous. The presence of biofilms has been shown to exist in implanted devices used in the dialysis community, in fluid pathways of haemodialysis machines and in other fluid pathways in connection to the dialysis community. Biofilms in the dialysis community will be reviewed and discussed from different aspects such as the process of biofilms formation, the biofilms on surfaces in clinical settings, visualization of biofilms and the control of biofilms.

B6 The effect of a synthetic furanone and disinfectants on Salmonella in biofilm

Lene K. Vestby og Live L. Nesse fra National Veterinary Institute, Section of Bacteriology, Oslo; Jessica Lønn-Stensrud og Anne Aamdal-Scheie fra University of Oslo, Department of Oral Biology, Oslo; Trond Møretrø og Solveig Langsrud fra Nofima Mat, Aas; Tore Benneche fra University of Oslo, Department of Chemistry, Oslo.

Contaminated feed and feed ingredients with Salmonella is a well-known problem and the feed industry is using large resources in the attempt to obtain feed and feed products without Salmonella. Our investigations have shown that some Salmonella clones seem to be able to persist in factory environments for several years. One way for Salmonella to persist in the feed factory environment is in a biofilm and we found that Salmonella serovars commonly isolated from factories were in general good biofilm producers at room temperature. We also found that Salmonella in biofilm is less sensitive to disinfectants than their planktonic counterparts.

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In several bacterial species, it has been shown that biofilm production is regulated by quorum sensing, i.e. the production and recognition of chemical signalling molecules that enable them to communicate within and between species and to behave in a multicellular way. Furanones are believed to inhibit bacterial colonisation and biofilm development through interference with bacterial quorum-sensing pathways like the AHL regulatory system and the AI-2 signalling system. In Salmonella, we found no evidence that biofilm production at room temperature seem to be regulated by either the AHL or AI-2 system. However, a synthetic (Z)-5-bromomethylene-2(5H)-furanone reduced biofilm production at room temperature in a number of Salmonella wild type strains, without affecting bacterial growth. By combining this furanone with conventional disinfectants (hypochlorite and benzalkonium chloride) the effect of the disinfectants on Salmonella in biofilm were significantly enhanced. The results show that furanones may prove to be valuable future weapons in the fight against Salmonella.

B7 Disinfectant Application Techniques in the Pharmaceutical Industry

Karen Rossington, Chield Medicare, UK

Many factors need to be considered when selecting a disinfectant for application in a pharmaceutical cleanroom environment, not just microbial activity. Limited information and guidance is available in GMP regarding the selection and use of disinfectants and this presentation discusses some of the advantages and disadvantages of the different disinfectants available.

Other factors need to be considered as well as microbial efficacy and this presentation looks at all the factors necessary to ensure the effective introduction of a new disinfectant, including health and safety, effect on the environment, format of use and support of the manufacturer.

The presentation also discusses the use and application of disinfectants and cleaning agents and shows how something as simple as the choice of format a disinfectant is supplied in can have an effect on the efficacy of the decontamination programme.

No current disinfectant validation programme can go ahead with consideration to the impact of European legislation such as the BPD and REACH. The presentation will give an update on the current situation with regards to public area disinfectants.

GENERAL

B8 Reading the runes; Demystification of disposable glove legislation*Nick Gardner, Shield Scientific*

The use of disposable gloves in the cleanroom environment is widespread. Indeed they are such a big part of our working lives that overall glove usage in the US has dramatically increased from less than 1 billion to over a 20 billion. We tend to use disposable gloves primarily for process protection from human-borne contamination. However increasingly within the pharmaceutical, biotechnology and medical device industries, the need for personal protection from chemical splashes, biohazards etc is equally important. As safety in the cleanroom environment becomes an increasing concern, do we really understand what level of protection we are getting?

B9 Integrated automatic Water Intrusion Test with thermal compensation on an autoclave*Stefano Gandini (De Lama)*

Reliable integrity testing of critical vent filters is a fundamental step in sterility assurance. The integration of the Water Intrusion Test algorithms into the software of the autoclave eliminates the need for additional integrity test hardware thus reducing the validation effort.

It's a well known fact that temperature and temperature drifts interfere with integrity test results. The use of an integrated temperature probe inside the test water vessel avoids starting a test with too warm or too cold water. An additional temperature probe inside the compacted gas net volume allows for a mathematical compensation of the end test result hence giving a reliable test result even under rough environmental conditions.

De Lama evaluated the integrated Water Intrusion Test concept from Sartorius Stedim Biotech. During the development the test result accuracy was qualified with and without temperature drifts collecting water on a high precision balance. For highest accuracy the test algorithm used the applied test pressure and the atmospheric pressure to calculate the compacted gas net volume.

The outcome was a robust and highly accurate integrated Water Intrusion Test using few additional components and applicable on autoclaves or any other software based equipment.

CONTROLLED ENVIRONMENT IN INDUSTRY

B10 Renhet inom verkstadsindustrin*Tommy Nordkil, Volvo technology Corporation*

During the Second World War, the war industry started taking interest in cleanliness. In the early 50'ies the civilian industry took after.

The probably most important driver was mass production that required an improved cleanliness.

When setting cleanliness requirements for mechanical products most common is to specify the particle cleanliness of parts and components. It is not common that cleanliness requirements are specified for the working area. When it is, the reasons usually depends in making it possible to fulfil a requirement specified for a part or component surface.

Today many mechanical industries still do not have any knowledge concerning cleanliness testing. Neither have they equipment to perform cleanliness tests.

B11 Erfarenheter från industriellt renhetsarbete*Jan Skogsmo, Swerea, IVF, Sweden*

Många företag kommer på allvar i kontakt med renhet när deras kunder kräver att komponenterna ska hålla en viss renhetsklass. Då gäller det visa vad detaljerna har för renhet och att de förhoppningsvis klarar kraven. För detta krävs en relevant analysprocedur anpassad för respektive komponent så man säkerställer att resultatet är representativt. Om detta bör kund och leverantör vara överens. En olämplig procedur kan lätt ge helt missvisande resultat. Det kan också bli onödigt komplicerat att utföra utan att ge något mervärde utöver en förenklad procedur.

Om partikelmängden överskrider kravnivån krävs åtgärder. Det är sedan viktigt att lista processkedjan och lokalisera de viktigaste föroreningskällorna. Innan andra åtgärder sätts in bör man gemensamt med kunden diskutera om kravnivån är relevant eller om den är onödig sträng.

Renhetskrav som inte ger något mervärde till produkten bör undvikas. Om man inte har något definierat renhetskrav är en lämplig utgångspunkt att fastställa den aktuella nivån och sedan säkerställa att denna nivå kan hållas utan plötsliga avvikelser. Ibland kan det räcka med ganska enkla åtgärder för att förbättra renheten. Om det inte räcker eller är möjligt med ändringar i produktionskedjan kan det behövas effektivare tvättprocess. Tvättmaskiner fungerar olika effektivt beroende på komponenternas geometri och på vilka volymer som tillverkas. Det är därför mycket viktigt att tvättprocessen är rätt anpassad för produktionen.

CONTROLLED ENVIRONMENT IN INDUSTRY

B12 Common language in Cleanliness Assessment.

Jan A.P. van Riet, SKF Göteborg, Sweden

Cleanliness is a quality issue and requires a common language in Cleanliness Assessment. No absolute methods are available for cleanliness assessment.

The cleanliness assessment standards ISO 16232 and VDA 19 recognize this by using the extraction curve to define the extraction procedure to measure the cleanliness level. The extraction curve describes the reduction rate of the cleanliness level of an extraction liquid applied to the test component in relation to time or volume. Variation has to be limited as much as possible to compare results. Procedures need to be agreed upon between customer and supplier.

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A13 Understanding ISO 21501-4

Gaetano 'Nino' Lattanzi, PhD, A.&L.CO. Industries, Italy

Under the title Determination of particle size - Single particle light interaction method ISO 21501 includes four standards related to the methodology for calibrating optical particle counters for air and for liquids (scattering and extinction type). Specifically, ISO 21501-4 provides a calibration procedure and verification method for airborne particle counters to minimize inaccurate measurements and reduce variations between different instruments. These new guidelines require pulse height analysis (P.H.A.) for particle counter calibrations, which reduce inconsistencies. The presentation covers the different requirements of the new standard and the differences/compliances with the already well known current calibration procedures.

A14 Viable and non viable environmental monitoring strategy for real time release in pharma industry

Gilberto Dalmaso in A.&L.CO Industries, Italy

The scope of this presentation is to show the usefulness and potentialities of this new rapid microbiological technology/method implemented in the pharmaceutical field in viable and non viable environmental monitoring strategy for real time release in pharma industry and in particular applied on the manufacturing process investigation, using the real-time evaluation, to engage the suitable corrective actions and resolute remedy at the right time.

This application has been fundamental to solve an important problem in a short time against the microbiological traditional method resolution, regarding the manufacturing process, which allowed discover and identify considerable benefits. Every day the samples have been analysed in real-time and

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these results provided a useful mapping of all critical points contaminated to allow the specific actions implementation, reconsider the numbers and type of environmental monitoring and re-samples and which type of sanitization carry out to remove the problem. It is important to underline that the new technology has been able to provide economical benefits in terms of "safe-costs" and the "stock-out" risk reduction of the products as well.

Moreover the case study reported has also been useful to implement the process understanding evaluation related to the test carried out in the laboratory until now. This means that in a lot of other fields and other type of analyses this rapid microbiology and the correlated technology could be implemented to improve the quality of the process and the risk of management.

A15 USP<1223> Validation Tests of a Realtime Microbial Detector and Suggestions for Implementation in Environmental Monitoring

Jianping (J.P.) Jiang, BioVigilant Systems, Inc, USA

An optical-based airborne microbial detection instrument, BioVigilant's IMD-A system, has been designed for real-time environmental monitoring. The instrument detects airborne microbes, using the intrinsic fluorescence produced by their biological markers (e.g. NADH and riboflavin for vegetative cells and dipicolinic acid for spores). The intended applications include pharmaceutical and hospital aseptic facilities. In order to validate the IMD-A instrument for its capability of detecting airborne bacteria, a series of prescribed USP<1223>tests were completed in a test chamber using aerosolized bacterial cells and spores, in which the IMD-A instrument and a conventional viable microbial air sampler (Andersen 6-stage sampler) were operated side-by-side. Five microorganisms, *Bacillus atrophaeus* spores, *Escherichia coli*, *Staphylococcus epidermidis*, *Micrococcus lylae* and *Corynebacterium afermentans*, were aerosolized and measured by both instruments. The test results will be presented.

The presentation will also outline a proposed site validation roadmap for IMD-A implementation in an aseptic facility as an environmental monitoring tool for contamination control.

PANEL DISCUSSION

A16 Safety of APIs and Medicines against Counterfeits

In the panel: Tor Gråberg, Kathryn King, Gerry Prout and Anders Ulfhielm.