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PDA Pharmaceutical Manufacturing & Quality Conference 2023 strives to optimize guidelines and practices

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The conference convened global industry leaders and experts to discuss innovations, trends, technologies and new regulations transforming pharmaceutical manufacturing

The PDA Pharmaceutical Manufacturing & Quality Conference was held in **Singapore on 15 and 16 August 2023.** To achieve the strong objective of reshaping the future of pharmaceutical manufacturing, the conference was themed " **The Way Forward: Trends, Technologies and New Regulations Transforming Pharmaceutical Manufacturing** ". Following the implementation of revised Annex 1, the PDA held multiple sessions to share industry tips and lessons learned.

PDA Pharmaceutical Manufacturing & Quality Conference 2023 provided delegates with a great opportunity to network and collaborate on innovative projects, discover potential partnerships with fellow professionals. To further improve contamination control measures in aseptic areas of pharmaceutical manufacturing, GMP Annex1 has been revised twice, first in August 2022, and now in August 2023.

A two-day conference covered pressing issues and current trends with extensive presentations, interactive panels, and thought-provoking sessions. The forum convened global industry leaders and experts to discuss innovations in pharmaceutical manufacturing. A total of 180 delegates participated in the forum to enlighten 36 eminent speakers alongside 17 exhibitors who showcased innovative technologies, products, and solutions.

In addition, an industry networking reception was an opportunity for pharmaceutical manufacturing and quality representatives to share ideas and explore innovations with peers, speakers, sponsors, and exhibitors.

Pharmaceutical Manufacturing & Quality Conference highlights:

The PDA facilitates quality risk management through a systematic approach to documentation. A key objective of the forum was to assist regulators and industry to make better informed decisions concerning drug quality and substances across the pharmaceutical lifecycle through application of quality risk management principles and tools.

An eclectic interdisciplinary audience across Biomonitoring, Biotech supervisors, Microbiologists, Production Managers, Quality Assurance Managers, Research & Design Specialists, Regulators, Consultants, and many others participated in these enthralling sessions. A series of presentations covered Vaccine Production, Quality and Regulatory Compliance, the recent updates to Annex 1, Supply Chain/CDMOs/Outsourced Operations Management, Microbiology/EM, ATMP/Cell & Gene Therapy, Digitalization/AI, as well as trends, technologies, and new regulations transforming pharmaceutical manufacturing. Extensive and informative product demonstrations from Merck and Charles River Laboratories enhanced the delegates' experience.

An exclusive “PDA Distinguished Service Award” was presented to Samuel Tan from Novartis in recognition of his contributions and service to PDA. Dr. Hue Kwon, Head Of Quality at Samsung Bioepis has also been appointed to join the Regulatory Affairs and Quality Advisory Board (RAQAB) Board alongside Dinesh Khokal who is also the Director of External Affairs & Quality Administration at Amgen.

Many seamless panel discussions and Q&A sessions engaged the audience. The panelists discussed agility and adaptability as essential components of being future-ready for pharmaceutical manufacturing through digital transformation. A further emphasis was placed on digitally-driven insights and incorporating the cutting-edge future-proof perspectives for process improvement.

Strategies for Sustainable Compliance:

Rick Friedman, Deputy Director of the Office of Manufacturing Quality within the Office of Compliance for the US FDA/CDER, opened the conference's first day with a presentation on ‘*Strategies for Sustainable Compliance*’. Friedman stressed the factors that can affect product quality and availability during the drug manufacturing lifecycle, including Manufacturing process variation and state of control; Manufacturing facilities and equipment; and Oversight of outsourced activities and suppliers.

Sharing key insights from the recently revised ICH Q9 guideline in Annex-1, Friedman explained “An effective pharmaceutical quality system drives both supply chain robustness and sustainable GMP compliance. The pharmaceutical quality system, including management responsibilities, also uses quality risk management and knowledge management to provide an early warning system that supports effective oversight and response to evolving quality/manufacturing risks from the pharmaceutical company or its external partners.”

In addition to recommending a structured investigation process with a goal of identifying the root cause, Friedman suggested that digitalization, automation, semi-continuous or continuous manufacturing, building management systems, and 100% inspection technology could be used to achieve sustainable compliance. A further adaptation of ‘Rapid Testing and Monitoring Technologies’, as well as the use of robotics, were considered having potential to significantly reduce quality and safety risks in aseptic processing.

Regulatory and Compliance insights concerning Vaccines Production:

Aaron Allen, Director, Global Quality Moderna, discussed "Challenges and Solutions to Development and Scale-Up of mRNA Platform Products". Allen assessed the novel innovative approaches and procedures for optimizing mRNA vaccine development. As part of the accelerated development process, Allen proposed Control Strategies for reducing sources of variability, such as Critical Quality Attributes Identification (CQA), Process Parameter Correlation (PPC) along with effective analysis of failed processes. Allen reiterated that the qualification of processes across scales further reduces the risk of parallel activities and facilitates the process design, performance qualification, and continual process verification at multiple scales, which will be useful for variant scalability.

Legal Implications of Cross Contamination in Vaccine Manufacturing:

Jay Jariwala, Senior Director, Regulatory Compliance, discussed the legal implications of cross-contamination on cGMP regulations to prevent contamination (viral, physical, chemical) of container/closure during drug production. He addressed the effects of cross contamination in the vaccine manufacturing industry in relation to the current enforcement trends at the Center for Drugs Evaluation and Research (CDER). A key focus was on accountability for investments, human resources, R&D, and disposal of waste materials. As part of the control process, production downtime affects manufacturing capacity, market withdrawals, and sample availability. Jariwala stressed that cGMP-regulated buildings must provide ample space for equipment, operate in defined areas, and document procedures in detail.

Establishing Analytical Methods for Emerging mRNA-based Therapies:

Dr. Huixing Feng, Merck's Senior Technical Expert, discussed the potential applications of mRNA-LNP vaccines and therapeutics, including prophylactic vaccines, therapeutic vaccines, and cell and gene therapies. To demonstrate safety, potency, and purity of mRNA vaccines, she explained robust analytical methods in addition to mRNA vaccine regulatory considerations, and the quality control extension to the entire mRNA substance. Additionally, she recommended Liquid chromatography–Mass spectrometry (LC-MS) analysis for mRNA as well as enabling LC-MS methods for batch release testing and stability testing in GMP environments. For enhanced decision-making, she advocated combining platform approaches with product-specific methods. Data-rich techniques such as Next Generation Sequencing (NGS) and LC-MS facilitate more depth of characterization.

Points to Consider(PtC) for Manufacturing Advanced Therapy Medicinal products (ATMPs):

Andiyanto Sutandar, Consulting Director at NNIT Singapore and *Richard Denk Senior Consultant Aseptic Processing & Containment SKAN AG* discussed PtC for the Manufacturing of ATMPs in line with the new Annex 1 implementation guidelines. IAround 16 different topics are included in the content of the PtC for the manufacturing of ATMPs. Richard Denk emphasized the importance of primary containment control when manufacturing ATMPs, including closed systems, bio safety cabinets (BSCs) with single-use systems, isolators, and other factors. The Pros and Cons of PtC for ATMP manufacturing were debated, along with Biosafety recommendations for preventing cross contamination.

Virtual Reality (VR) Training System to Standardize and Increase Quality:

Johnson & Johnson's Director of Aseptic Processing, Dieter Bachmann, and *Molly Ting, Director, Global Process Owner of Pharmaceutical Quality & Compliance Training*, presented insights on integrating human psychology with VR technology in order to create a valid training system for GMP operators in sterile manufacturing. A session titled 'Human Operator 4.0' discussed VR training systems as a means of standardizing, increasing quality, and enabling faster onboarding.

Aseptic Processing with New Technologies, Closed Isolators and Gloveless Isolators:

Richard Denk, Senior Consultant Aseptic Processing & Containment at SKAN AG, shared insights about revised Annex 1 and its impact on different isolation technologies (open or closed), surface decontamination, gloves on isolation, and gloveless isolation. To achieve a comprehensive contamination control strategy, he emphasized the importance of using a traditional isolation line and filling line, an automated isolation line, and most importantly, a fully digitalized/AI and gloveless robotized filling isolation line. As an enabler of a holistic Contamination Control Strategy (CCS) approach, he recommended using robots in aseptic areas to install filling pathways, monitor environmental conditions, load and unload lyophilizers, and individually customize containers.

Day Two of the conference addressed tactical approaches for Contamination Control Strategy (CCS) Implementation.

Beginning with Microbiology and Remote Environmental Monitoring and Management (RMM) sessions by *Emily Cheah, Senior Managing Director Of Charles River Laboratories.* In addition, *Ziva Abraham, CEO of Microrite* outlined the key remedial steps necessary to prevent contamination events from occurring again. To implement effective corrective and remedial actions, she recommended researching new investigative processes and mapping out the ingress and transport paths of contaminants and prevention.

Furthermore, *Jim N Polarine Jr., Senior Technical Service Manager at STERIS Corporation*, explained that in order to achieve high levels of control within a cleanroom, techniques such as Triple Cleaning, 9X Cleaning, Fogging, and Validation Components are essentials as part of Environmental Monitoring and Disinfectant Validation process. He mentioned that Holistic CCS is a major principle of the EU Annex 1 revision. Also, *Senior Microbiology Consultant at ValSource, Kim Sobien* recommended ‘Holistic Contamination Control’, stating that the Annex 1 illustrates interdependence in CCS elements and links them together. Sobien discussed elements of CCS which include design, premises, equipment, process validation,

outsourcing management, sterilization validation, utilities, raw material control, containers & closures, vendor approval, and continuous improvement.

Role of Enzymatic Indicators (EIs) in Pharma Manufacturing:

James L Drinkwater, Head of GMP Compliance & Leader of PHSS Aseptic processing focus group and member of UK's Pharmaceutical Healthcare Sciences Society shared the role of Enzymatic Indicators (EIs) to improve efficiencies in Vaporized Hydrogen Peroxide (VHP) cycle development for Isolator barrier technology and associated GMP manufacturing applications. James explained how the revised Annex 1 encourages the use of new and alternative technologies for Quality Risk Management (QRM) following the science of aerosolization and dry fog by vH2O2/VHP and related bio-decontamination processes to achieve sterile environments in pharma manufacturing.

Revolutionizing Digitalization in Sterile Manufacturing:

Anil Kumar Yadav, Global Account Manager for Industrial Amazon Web Services, discussed trends affecting the pharma manufacturing industry, especially the use of artificial intelligence(AI) and machine learning(ML) for connected and sustainable digital databases that facilitate the assessment of business opportunities for pharmaceutical manufacturers. Recent trends include extensive use of AI and Machine Learning throughout the value chain, including R&D, Clinical development, manufacturing, supply chain, commercial, post-market surveillance, and patient support.

The importance of data integrity, changing environments, audit strategies, metrics, budgets, vulnerabilities, data governance, and digital technology compliance were stressed by *Scott Deckebach, Senior Director of Data Governance, Integrity and Digital Technologies Compliance at Lachman Consultant Services*. In order to build trust in data integrity, he stressed the importance of shifting from cGMP to risk orientation, demonstrating comprehensive data governance and controls. Besides integrating a holistic risk assessment process into each new technology adoption, he emphasized making Data Integrity an explicit objective.

General manager at Thermo Fisher Scientific (Patheon/CDMO), Selva G recommended leveraging Universal Data Intelligence to optimize machine parameters, reduce deviations, and enhance processes. He stressed the need to connect machines and devices with people in real-time to transform end-to-end operations using universal data intelligence. He cited successful digitization implementations including "Digital solution for Sterile Manufacturing OEE monitoring", "Advanced Analytics for OEE Uplift" and "Augmented Execution Systems (AES)" powered by Virtual Reality (VR) for Immersive Practical Training and Digital system implementation for added advantages.

Post-Conference Sponsored Workshop and investigations Bootcamp

An investigation bootcamp and post-conference workshop were organized following the conference to address 'Difficult Microbiological Excursions'. The half-day workshop explored microbiological investigation issues, including recurrent mold contamination, biofilm formation, viable but non-culturable microorganisms, and false positive results. Regulatory updates from *TR 89 with Priyabrata Pattnaik,* provided deeper investigation into areas of sampling, test methodology, and test suitability to uncover root causes of data deviations, rather than batch acceptability analysis. Participants acquired knowledge on technical specification and specialized competencies to conduct and document robust microbiological investigations. Additionally, participants investigated mold, biofilms, and viable but non-cultivable organisms in real-life case studies.

Upcoming PDA events:

PDA Asia Pacific is gearing up for its final two conferences of the year in 2023. First up is the **2023 PDA Aseptic Processing of Biopharmaceuticals Conference**, set to take place in Incheon, South Korea, from October 31st to November 1st, 2023. Following that, the **2023 PDA Asia Pacific Regulatory Conference** is scheduled for November 28th-29th, 2023, in Melbourne, Australia.