2022 PDA Annex 1 Workshop
Amsterdam / The Netherlands
22-23 September 2022

Thursday, 22 September 2022

09:00	**Welcome and Introduction**	Falk Klar, *PDA Europe*
09:05	**Welcome Remarks from the Workshop Leaders**	Marcia Baroni, *Emergent BioSolutions* Richard Denk, *SKAN*
	P1: Overview of and Revision Process for Annex 1 *Over the past four years, the new Annex 1 has gone through multiple sets of industry review comments, and revisions. The current version presents a diverse, international perspective on regulatory expectations, recommendations, and requirements for modern sterile drug and biologic product manufacturing. The revised Annex 1 contains a significant amount of new and more detailed content on many topics. It places a heightened emphasis on the use of risk-based assessment and approaches to design and evaluate manufacturing contamination control. This session will provide insights from both the regulatory authorities and industry experts involved in the Annex 1 development and review process of the revision, with a focus on the evolution, planning, and implementation of these changes.*	**Moderator:** Patrick Nieuwenhuizen, *PharmaLex*
09:20	**Regulatory Perspective** Insights from the perspective of the regulator on Annex 1. There were 4 main topic areas that received the bulk of the comments which will be touched on in this discussion.	**Presenter:** Paul Gustafson *PIC/S pre-recorded presentation*
09:40	**Insights from a Former Regulator** Insights from the perspective of the regulator on Annex 1. There were 4 main topic areas that received the bulk of the comments which will be touched on in this discussion.	**Presenter:** Tracy Moore, *TM Pharma Group Ltd*
10:00	**Q&A; Discussion**	
10:45	**Coffee Break, Poster Sessions & Exhibition**	
	P2: Scope, Principles, and Pharmaceutical Quality Systems *This session opens our in-depth look at the content of Annex 1. The Scope, Principles and Pharmaceutical Quality System sections introduce the Vision of the Annex 1 changes that track through all other sections. This session will highlight Annex 1 focal points including Contamination Control Strategy, Quality Risk Management, and Quality culture, including a discussion on the importance of human factors: knowledge, attitude, and experience. This session will also address the expanded scope of Annex 1 to include some non-sterile.*	**Moderator:** Frederic Ayers, *Eli Lilly and Company*
11:15	**Using Quality Risk Management to Enable the Contamination Control Strategy** The application of risk management and risk principles has been identified in Annex 1 as a foundational element for developing a robust contamination control strategy (CCS). Overall CCS goals would include a	**Presenter:** Patrick Mains, *ValSource Inc.*

	definition of critical control points, evaluation of control effectiveness and technical/process knowledge are all factors that can be integrated into robust risk activities. This session will evaluate the language used the Annex 1 uses to describe risk activities, where those activities are required, and explore risk assessment tools that will enable the contamination strategy goals.	
11:35	**Contamination Control Strategy Development** The development and documentation of the Contamination Control Strategy are viewed by many as the most difficult new requirement in the Annex 1 revision. This session will address how to fulfill this requirement, with a discussion on the expectations from regulators and practical advice derived from the industry.	**Presenter:** Cheryl Essex, *Sanofi*
11:55	**Considerations of Annex 1 for Advanced Therapy Medicinal Products and Low Bioburden Products** With the publication of EU GMP guideline Part IV: GMP requirements for Advanced Therapy Medicinal Products (Guidelines on Good Manufacturing Practice specific to Advanced Therapy Medicinal Products), there are discussions in the industry if Part III: Annex 1: "Manufacture of Sterile Medicinal Products" is still applicable for ATMPs. The purpose of this session is intended to provide clarity in terms of regulatory requirements vs examples of best practices that can be utilized from Annex 1 during the manufacture of ATMPs. PIC/S Annex 2A would also be discussed with an aim to understand legal and technical applicability and how it can be used to bridge requirements and support a consistent approach that is as jurisdiction-wide/agnostic as possible.	**Presenter:** Biswarup Dasgupta*, Vertex Pharmaceuticals*
12:15	**Q&A; Discussion**	
12:30	**Breakout Session 1** *Attendees will discuss the implementation challenges, and what can be done to meet those challenges, associated with the topics presented in P1: Overview of and Revision Process for Annex 1 and P2: Scope, Principles, and Pharmaceutical Quality Systems.*	
13:10	**Lunch Break, Poster Sessions & Exhibition**	
	P3: Premises and Barrier Systems *Aseptic manufacturing facilities come in a variety of shapes and sizes, from traditional aseptic through restricted access barrier systems (RABS) and Isolators. This session will look at some of the key design and operational aspects that have been impacted by the revised Annex 1.*	**Moderator:** Marcia Baroni, *Emergent BioSolutions*
14:10	**Cleanroom Design: Classification, Qualification, Air Visualization** Cleanroom design is a critical balance of engineering and operational processes that are required to meet regulatory guidelines. This session will provide considerations for meeting those requirements and maintaining a clean room.	**Presenter:** Frederic Ayers, *Eli Lilly and Company*
14:30	**Cleanroom Operation: Disinfection, Transfer of Materials, Monitoring** Annex 1 changes reflect a distinction between cleaning and disinfection, acceptance of supplier-approved documentation for ready-made disinfectants, and improved clarity of the ownership of disinfection validation. The proper use of sterilization or disinfection for the transfer of materials has also been clarified, along with specific instances where	**Presenter:** David Keen, *Ecolab*

	microbiological monitoring is recommended. This session will facilitate discussion for improved understanding and approaches for these changes.	
14:50	**Barrier Technologies: RABS and Isolators, Glove Integrity, Robotics Decontamination** Barrier technologies, such as RABS and isolators, are mentioned 32 times in the revised Annex 1 and their use should be considered in the contamination control strategy. Besides barriers, glove management and the integrity of the gloves should be demonstrated. A validated decontamination cycle using vaporized or nebulized hydrogen peroxide, as well as a robotics system to minimize manual intervention, will be presented.	**Presenter:** Richard Denk, *SKAN*
15:10	**Q&A; Discussion**	
15:25	**Breakout Session 2** *Attendees will discuss the implementation challenges, and what can be done to meet those challenges, associated with the topics presented in P3: Premises and Barrier Systems.*	
16:05	**Coffee Break, Poster Sessions & Exhibition**	
	P4: Equipment, Technology, and Utilities *This session will discuss the impact of the Annex 1 revision on aseptic manufacturing facilities, specifically focusing on equipment design, indirect product contact parts, such as stopper bowls, and critical utilities, such as water systems.*	**Moderator:** Richard Denk, *SKAN*
16:35	**Decontamination and Sterilization of Direct and Indirect Product Contact Surfaces** The uncertainties surrounding the sterilization of direct and indirect product contact surfaces have been a hot topic since the first publication of the draft Annex 1 in 2017. While intuitively there is no question it should be done when it comes to indirect contact parts in an isolator environment, the practical and logistical implications are numerous, especially when you introduce the option of surface decontamination. This session will focus on different options and points to consider when making the right selection for your process.	**Presenter:** Marcia Baroni, *Emergent BioSolutions*
16:55	**Water Systems and Other Critical Utilities** The Annex 1 revision specifies a totally new section regarding “utilities” with a special focus on water, process gases, and steam of pharmaceutical grade. This presentation will discuss key changes in the water and other critical utility systems requirements, providing an interpretation of the new chapter requests, in light of current industry practice.	**Presenter:** Paolo Curtò, *DOC Validation – MASCO GROUP*
17:15	**Q&A; Discussion**	**Moderator:** Richard Denk, *SKAN*
17:30	**Breakout Session 3** *Attendees will discuss the implementation challenges, and what can be done to meet those challenges, associated with the topics presented in P4: Equipment, Technology, and Utilities.*	
18:10	Closing Remarks from Day 1	Falk Klar, *PDA Europe*

18:30 - 20:00	**End of Workshop Day 1, Networking Reception**	

Friday, 23 September 2022

08:00	**Welcome and Day 1 Report Out**	**Moderator:** Marcia Baroni, *Emergent BioSolutions*
	P5: Personnel Training, Qualification, Gowning, and Monitoring/Assessment *Training and qualifying operators are of critical importance to ensuring proper aseptic technique and cleanroom behavior. Routine monitoring of personnel ensures that the qualified personnel is following the established procedures and that they can meet the strict gowning cleanliness requirements during normal operations. Trending and analysis of gloves and gown EM data can provide critical feedback on individual operator performance, potential routes of contamination, specific gowning procedures and overall training efficacy.*	**Moderator:** Kurt Jaecques, *GSK*
08:20	**Qualification and Training** The revised Annex 1 draft has significantly increased the depth and breadth of requirements surrounding personnel qualification and training. However, are these truly new requirements, or has there simply been a formalization of pre-existing industry practices? Join us for a discussion of these requirements and what it means for your operations, as well as exploring some options for implementation.	**Presenter:** Patrick Nieuwenhuizen, *PharmaLex*
08:40	**Gowning, Personnel Monitoring, and Beyond** The Annex 1 revision has added more details to an already prescriptive set of requirements on personnel gowning and monitoring. In this presentation, the explicit new expectations will be reviewed and the broader Annex 1 theme of personnel awareness and monitoring beyond the contact plate will be discussed.	**Presenter:** Cheryl Essex, *Sanofi*
09:00	**Q&A; Discussion**	
09:15	**Breakout Session 4** *Attendees will discuss the implementation challenges, and what can be done to meet those challenges, associated with the topics presented in P5: Personnel Training, Qualification, Gowning, and Monitoring/Assessment.*	
09:55	**Coffee Break, Poster Sessions & Exhibition**	
	P6: Production Technologies, Part 1 *This session will focus on the Annex 1 requirements for aseptic processing and filtration of sterile products. The aseptic processing discussion will address the types of operations and grades needed for aseptic preparation and processing operations. The filtration and sterilization presentation will provide insight into the different types of sterilization and the parameters needed to demonstrate success.*	**Moderator:** Patrick Mains, *ValSource Inc.*
10:25	**Aseptic Processing**	**Presenter:**

	This presentation will provide clarity on some of the changes related to aseptic procession simulation (APS) as it is important to note the proposed addition of "a demonstrated aseptic proficiency in the performance of aseptic process activities" in place of the requirement for "participation in a successful APS" is not designed to exclude the use of APS.	Frederic Ayers, *Eli Lilly and Company*
10:45	**Filtration and Pre-use Post Sterilization Integrity Testing** This presentation will highlight the use of risk-based assessments (as noted in the PDA consortium publications) to determine what controls are needed to mitigate and prevent filter-related risks, where Pre-Use Post Sterilization Integrity Testing (PUPSIT) is determined to be a sound (or appropriate) method for risk mitigation and process control, along with considerations to better design and control the PUPSIT process.	**Presenter:** Thao Vinh Le, *GSK*
11:05	**Q&A; Discussion**	
11:20	**Breakout Session 5** *Attendees will discuss the implementation challenges, and what can be done to meet those challenges, associated with the topics presented in P6: Production Technologies, Part 1 (Aseptic Processing and Filtration and Pre-Use Post Sterilization Integrity Testing).*	
12:00	**Lunch Break, Poster Sessions & Exhibition**	
	P7: Production Technologies, Part 2. *This session will introduce some of the more intriguing topics covered and expanded in the revised Annex 1, which were selected based on input from the sterile product manufacturing community, as noted during prior meetings and discussions.*	**Moderator:** Frederic Ayers, *Eli Lilly and Company*
13:00	**Container Closure Integrity Testing and Finishing** Annex 1 changes reflect more prescriptive recommendations for testing container closure integrity (CCI) of finished products. Ampules are no longer the only containers suggested for 100% "leak testing." The inclusion of flexible bags for 100% leak testing is a significant new recommendation that will be challenging to meet for users and flexible container suppliers. Validated methods for leak tests are now prescribed, as well as concrete language for validation of CCI for transport and shipping. For container types not specifically mentioned in Annex 1, guidance is given that testing programs should be based on knowledge of the container closure system and the process being used, implying that robust CCI data should perhaps be available from development and scale-up activities. This presentation will facilitate discussion for improved understanding and approaches for these changes reflecting CCI testing.	**Presenter:** Derek Duncan, *Lighthouse Instruments*
13:20	**Production and Specific Technologies (Blow-Fill-Seal, Lyophilization, Single Use System, and Terminal Sterilization)** Annex 1 outlines several technologies for filling and finishing sterile products, among other Blow-Fill-Seal and lyophilization. Equipment and facility design and (in-process) controls are important aspects that contribute to the overall sterility assurance of the finished product. This session will outline some points of attention when it comes to (aseptic) filling using BFS and lyophilization technology. It zooms in on terminal sterilization of products, or better the limitations of terminal sterilization and requirements for aseptic manufacturing where terminal sterilization	**Presenter:** Patrick Nieuwenhuizen, *PharmaLex*

	is not possible. Prevention of contamination is key in aseptic manufacturing and the session will discuss the use of Single-Use Technology versus stainless steel set-ups, with their respective pros and cons.	
13:40	**Q&A; Discussion**	
13:55	**Breakout Session 6** *Attendees will discuss the implementation challenges, and what can be done to meet those challenges, associated with the topics presented in P7: Production Technologies, Part 2 (Container Closure Integrity Testing and Finishing and Production and Specific Technologies (Blow-Fill-Seal, Lyophilization, Single Use System, and Terminal Sterilization)).*	
14:35	**Coffee Break, Poster Sessions & Exhibition**	
	P8: Aseptic Process Simulation/Environmental Monitoring *APS has been identified as one of the key aspects of aseptic process control and monitoring. This session will review the related changes and begin discussing the interpretation and implementation of these recommendations and requirements. The presentations will focus on the Annex 1 requirements for APS (media fills) and environmental and process monitoring, including the new requirements and considerations for qualifying and operating a clean area and the extensive new requirements needed to successfully validate an aseptic process.*	**Moderator:** Cheryl Essex, *Sanofi*
15:05	**Environmental and Process Monitoring** The importance of a firm's EM program to support and provide direct feedback on a given contamination control strategy is a renewed focus in the Annex 1 revision. This presentation will highlight some of the changes and areas of consideration and will discuss the implementation of EM risk assessments, the importance of appropriate monitoring equipment, monitoring during various operational conditions, and data trending. The challenges of increased personnel monitoring and utilization of rapid microbiological methods will also be addressed.	**Presenter:** Kurt Jaecques, *GSK*
15:25	**Aseptic Process Simulations** A proper design and implementation of Aseptic Process Simulation are key to supporting the verification of the capability of the overall manufacturing process to prevent product contamination. The objective of this presentation is to review and clarify the comprehensive set of new requirements and expectations that are listed in the revised Annex 1.	**Presenter:** Biswarup Dasgupta*, Vertex Pharmaceuticals*
15:45	**Final Panel Discussion**	**Moderator:** Cheryl Essex, *Sanofi*
16:30	**Day 2 Report Out**	**Moderator:** Marcia Baroni, *Emergent BioSolutions*
16:50	**Closing Remarks & Farewell**	Falk Klar, *PDA Europe*
17:00	**End of Workshop**	