



The Parenteral Drug Association Italy Chapter presents

Manufacturing trend of parenterals: a glance to the future

Bari, 5th and 6th of October 2017, Hotel Parco dei Principi

Speakers Abstracts

Abdelaziz Toumi – Merck KGaA

Title: Biotech & Pharma Trends and their impact on manufacturing and supply

The technical & business complexity of biopharma is increasing. The world-population is growing and so access to affordable medicine. Digitalization has reached our industry and is becoming a key strategic opportunity to build new competitive advantage(s). New modalities are leading to personalized as well as to more complex biologics calling for more innovative manufacturing processes and overall new business model(s).

To address these challenges, the biopharma industry needs to invest more into optimizing the development process, our innovation cycles and leveraging on cross-industry collaboration. Key success factor is an integrated end-to-end approach to process development from R&D, through manufacturing until commercial operations.

After presenting the key challenges and trends that our industry is facing (internal as well as external factors), two industry relevant case studies are going to be discussed 1) an approach to enhance the development process from early discovery to commercialization which enable us to serve extremely shortened timelines into clinics and commercial launches, and 2) how to build manufacturing innovation through right infrastructure, right people and mindset.

Michele Simone – Bracco Suisse S.A.

Title: Views on Quality System Advances and their Impact on Manufacturing of the Future

Drug makers have used cutting-edge science to discover medicines, but they have manufactured them using techniques dating to the days of the steam engine. manufacturing processes are falling behind other industries in terms of technology and efficiency. Now, the pharmaceutical industry is moving toward a major upgrade from batch to continuous production.

Regulation of the future will also need to meet these challenges, by incorporating new scientific information into regulatory standards and policies. Both industry and regulatory practices will need to be informed by the best techniques of risk assessment and quality management.

From this presentation, you will learn:

- The "Current State" and the "Desired State" of Pharmaceutical Manufacturing in the 21st Century
- Continuous improvement vs process understanding
- Types of "improvement"
- Risk-based and Integrated Quality System Orientation

Janmeet Anant – BioProcess Systems Alliance

Title: Overcoming Quality and Regulatory Challenges of Implementing Single-Use Pharmaceutical Manufacturing

Single-use pharmaceutical manufacturing has been widely adopted in development and clinical manufacturing. Even though these disposable technologies offer various benefits, there are still some challenges based on a lack of standardization of quality tests and procedures.

From this presentation, you will learn:

- Current and upcoming industry and regulatory requirements for single-use pharmaceutical manufacturing systems
- Detailed compatibility requirements, including extractables/leachables, particulates, integrity and supplier change control standard proposals
- Quality and regulatory documentation based on these requirements, making the implementation of single-use systems more efficient

Mauro Giusti – Eli Lilly Italia

Eli Lilly Italia, Sesto fiorentino Plant, started a journey with isolator technology together the conversion of manufacturing plant from sterile and oral cephalosporins, to Insulin products filled in glass cartridges.

The journey involved setting up both isolators for sterility testing, which had been used previously, but also isolator for sterile filling, using high speed filling machines.

Interestingly this had not been the original choice of site management, but it was pursued based on the process to harmonize technologies across multiple sites.



At present not only Lilly Italia has reached the maximum level of productivity and quality with 2 high speed isolator lines for cartridges, but it is also preparing the acquisition of another isolator line for sterile filling of Fusion protein/MAB products in syringes.

The presentation will cover the journey of Lilly Italia toward a successful isolation technology and the learnings along the way

Massimo Mannini, Chiara Giani – GSK Vaccines

Title: Isolation and Disposable Technologies, Data Automation

How these transform Site Operations

Presentation will briefly summarize how the site is transformed in terms of Volumes, Technology, Data Management based on changes in Technologies leading to larger batches with comparison along the year of usage of RABS and moving to Isolation Technology

These basic transformations will lead the site to increase of batch sizes and consequent decrease of cost of goods, mainly driven by a better utilization of Human resources and reduction of Quality costs; costs are also impacted by introduction of disposable technologies and these additional changes are also leading to other consequences like requiring different skill and training mode for the operators and technical personnel.

Continuous changes in IT technologies is also leading to reduce human impact on Data Handling and data integrity issues by implementing control systems to reduce human impact on data

A brief and quick oversight that is leading the site to the e-BPR will be provided including the very difficult management of the mindset change

Final impact of all these evolutions are mainly driving the sites to change and adapt their Organizational Models, WoW and Governance together with competencies of all personnel required to run the operations and support functions

Annalisa Calvano, Elisabetta Matarrese – Merck Bar

According to current regulations, with particular reference to the FDA Guidance for Industry “Sterile Drug Products Produced by Aseptic Processing - Current Good Manufacturing Practice” and USP <1116> “Microbiological Control and Monitoring of Aseptic Processing Environments”, human intervention and personnel are the main source of contamination; its reduction is assured with application of engineering (isolator) and automation (validated cleaning and sterilization cycles).



Merck Bari site will adopt the strategy of filling under isolator technology, making it possible to perform the filling step in a more contained environment with a consequent reduction to the risk of contamination

Isolator technology is based on the principle of placing previously sterilized components (containers/products/closures) into a sterile environment. These components remain sterile during the whole processing operation, since no personnel or nonsterile components are brought into the isolator.

Isolator systems require relatively infrequent microbiological monitoring. Continuous total particulate monitoring can provide assurance that the air filtration system within the isolator is working properly. Surface monitoring within the isolator may also be beneficial on an infrequent basis. Being isolator technology pretty new, no clear guideline is available to define a fixed environmental monitoring program.

In any case, a comprehensive Environmental Monitoring program (particulate and microbial monitoring), based on the applicable sampling methodologies, as described here below, is essential in order to guarantee compliance of products with the Pharmacopoeial requirements for “Sterility” and “Foreign and Particulate Matter” in parenterals.

The use of isolator allow higher flexibility in media fill design compared to standard clean room. Relative risk and unique aspect of this technology are new challenges to be assess during aseptic process simulation and they should be taken into consideration when assessing the design of media fill. In particular, operator interventions are much less critical when using isolator compared to the inlet/outlet materials flow. Risk based approach should be used to define media fill strategy.

At the PDA Education, gain an understanding of strategy defined in Merck Bari for environmental monitoring program and media fill in the new vial isolator line and how they can be applied to demonstrated safety and facilitate pre-market review communications with the U.S. FDA and explore the comparison between the impact of total particulates and microbial contamination in ISO 5 environments /isolator vs aseptic operations).