Microbiology at the 11th PharmaLab 2023

20 November 2023 | Mycoplasma Detection Pre-Conference Workshop
21/22 November 2023 | Endotoxin and Pyrogen Testing, Alternative and Rapid Microbiological Methods, CGT/ATMP Quality and Safety

The conferences are part of PharmaLab
Analytics ▪ Bioanalytics ▪ Microbiology

Highlights

- Pharmacopoeial News in Microbiology
- Modern Alternative Systems and Methods – Rapid, Online, Real Time
- Regulatory Expectations
- Automation in Microbiology
- Recombinant Testing – Current Developments
- CGT/ATMP – Microbiological Control

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Background & Objectives of PharmaLab

2022, the first year after the pandemic, the 10 PharmaLab has attracted more participants to Neuss/Düsseldorf than ever before. With this success as a template, the 11th PharmaLab Congress will again be held on site in Düsseldorf/Neuss from 21-22 November 2023. The congress, which is aimed at employees and managers in all laboratory areas of the pharmaceutical industry, is composed of a pre-conference workshop, 6 international conferences from the fields of analytics, bioanalytics, microbiology and CGT/ATMP, as well as the accompanying exhibition. It will provide information on the latest developments in laboratory methods, systems, materials and the current status of regulatory requirements of pharmacopoeias and guidelines. In addition, experts from authorities, industrial quality control and contract laboratories will present their experiences with the use and qualification of analytical systems as well as with the validation of analytical methods and microbiological tests. Take advantage of this unique opportunity to learn about the state of the art in pharmaceutical laboratories and discuss current developments with speakers and colleagues.

4th International Mycoplasma qPCR Testing User Day
PharmaLab Pre-Conference Event

20 November 2023

Background & Objectives

Mycoplasma contamination of biopharmaceutical products (also known as biologics or large molecules) resulting from cell culture contamination in the manufacturing process poses a potential health risk to patients. Mycoplasmas can affect virtually every cell culture parameter with often only minor visible effects, creating an uncontrollable environment that is undesirable in the pharmaceutical industry. Therefore, regulatory agencies require manufacturers to test their biopharmaceutical products and to ensure the absence of mycoplasmas in released products. Most regulatory agencies have issued guidelines that provide protocols for mycoplasma testing, and some give recommendations for the validation of rapid NAT (nucleic acid amplification techniques) testing methods. This satellite symposium will give you a scientifically sound introduction into the field of Rapid Mycoplasma testing with a specific focus on NAT and more specifically on qPCR methods. It includes talks, case studies as well as interactive round table discussions from users to users.

Target Audience

The Pre-Conference Workshop is directed to responsible personnel involved in Quality Control testing of biopharmaceuticals and biologics, e.g.:

- QC Managers,
- Microbiologists, and Process Microbiologists
- Analytical Experts
- Biosafety and Pathogen Safety SME's
- Bioassay Developer
- Responsible Authority Employers

It is also useful for service providers, such as contract research organisations and contract manufacturers.

Moderation

Haidy Wafy, *Roche*

Speakers

Dr Alexander Bartes, *Roche*.
Senior Manager Global Analytical Science and Technology (gASAT).

Dr Thuy Bourgeois, *EDQM Strasbourg, France*.
Scientific Programme Manager, European Pharmacopoeia Department.

Yasmin Heynen, *Labor LS*.
Molecular Development.

Dr Caroline Kassim, *bioMérieux*.
R&D Bioscience Manager.

Jan-Oliver Karo, *Paul-Ehrlich Institut, German Federal Institute for Vaccines and Biomedicines*.

Marine Marius, *Sanofi Vaccines*.
Sr Scientist / New Vaccine CMC Analytical Leader - Microbiology platform Analytical Sciences Europe at Sanofi Vaccine.

Olga Müller, *Tetec*.
Head QC.

Dr Nicole Paland, *Minerva Biolabs*.
Head Product Development.

Programme

Current revision of Ph. Eur. chapter 2.6.7 Mycoplasmas and its impact on other Ph. Eur. Texts

- Aim of the current revision published in Pharmeuropa 34.2
- Work in progress: future revision of Ph. Eur. texts prescribing for the Mycoplasma text
- Case studies and perspectives

Dr Thuy Bourgeois, EDQM Strasbourg, France

NAT-based Methods for Mycoplasma Testing – Validation Strategy in the view of the Revision of the European Pharmacopoeia Chapter 2.6.7

- The challenge to correctly interpret the requirements for method validation and method suitability testing mycoplasma tests with NAT-methods
- Application-based experience with method validation, method suitability testing and routine testing of NAT-based mycoplasma testing as a user
- A suitable strategy for method validation and method suitability testing in a constellation of manufacturer, contract laboratory and customer (as an enduser)

Yasmin Heynen, Labor LS

Next Generation PCR Closed System Allowing for 1-Hour Mycoplasma Release Test of CGT Products

- A closed system sample-to-answer nucleic acid test that is designed to report the presence/absence of over 130 mycoplasma species in less than an hour with minimal hands-on time
- Currently, a double centrifugation sample preparation protocol (excluding cells) with LOD < 10 CFU/mL has been validated following current regulatory guidelines
- Taking into consideration the upcoming changes of the European Pharmacopeia - two new protocols that include cells in the test while providing the level of detection required to release CGT products:
  - a 10mL single-centrifugation protocol for testing larger volumes of product;
  - a low volume sample protocol for use when sample volume is limited.

Dr Caroline Kassim, bioMérieux

Development of a digital PCR-based Mycoplasma Detection Kit

- Issues of classic methods
- Possibilities of Digital PCR – Sensitivity, Accuracy Time Saving
- Detection < 10CFU of all Mollicutes (Mycoplasma, Acholeplasma, Spiroplasma) species

Dr Nicole Paland, Minerva Biolabs

Mycoplasma Real-Time PCR: Generic Method Validation of T-cell Culture

- Generic method validation acc. to Ph. Eur. 2.6.7 and 2.6.21
- Validation parameter evaluated: detection limit and specificity
- Application of a modified manufacturer's protocol

Alexander Bartes, Roche

Change of Mycoplasma NAT-bBased Method: Management of a Kit Discontinuation

- Implementation on mycoplasma NAT-based method on all our products: a successful journey but…
- Unexpected supplier kit discontinuation: how this situation was managed; what are the impacts?
- Selection & implementation of a new kit: return of experience

Marine Marius, Sanofi

Mycoplasma Testing & Evaluation for ATMPs – Lessons Learned!

- Comparison of SYBR-Green based and probe-based assay
- Challenges in method development & analysis
- Troubleshooting
- Method validation of a probe-based assay

Olga Müller, Tetec

Mycoplasma Testing – Experiences and Thoughts

Jan-Oliver Karo, Paul-Ehrlich Institut, German Federal Institute for Vaccines and Biomedicines

Congress Key Note

Main Conferences on 21/22 November 2023

Key Note on 21 November: The Impact on the Revised Annex 1 for Rapid Microbiological Methods Implementation

Dr Michael Miller

Key Note on 22 November: Preparedness in Pandemic Vaccine Manufacturing and Deployment

Prof Dr Isabelle Bekeredjian-Ding

Endotoxin and Pyrogen Testing
21/22 November 2023

Background & Objectives

Testing for endotoxins and pyrogens is a critical in-process and final release test for parenteral products. Over the past decades, various approaches have been developed to provide solutions for the wide range of products tested for endotoxins and pyrogens: RPT, LAL, MAT. With the LAL test method as an established, compendial methodology for bacterial endotoxins, including the harmonisation of EP, USP and JP, there is a solid basis for such testing. But the range of products to be tested is becoming broader and more complex as biotechnological and molecular biological techniques advance. Because of the importance of these tests, they are therefore under constant scrutiny by industry and regulators to ensure the effectiveness of the tests and the safe manufacture and release of products onto the market. Novel medicines such as cell and gene therapies and combinations with medical devices, as well as complex biopharmaceutical formulations, pose challenges for testing and require in-depth knowledge and expertise in the field of endotoxins and pyrogens. Furthermore, as the range of solutions offered by endotoxin testing vendors increases (e.g. recombinant factor C, ELISA-based test kits, automated LAL cartridge technology), it is important to gain a data-driven understanding of the benefits and limitations of each approach. Therefore, it is not only the discussions on low endotoxin recovery and endotoxin masking that are important. We should also focus on the need for future innovations within BET that provide solutions to current challenges with modern pharmaceutical and biopharmaceutical products for daily testing. In addition, automated solutions will play an important role, making issues of computer validation and data integrity important.

This conference will inform you about current developments in Endotoxin and Pyrogen testing, implementation of new methods as well as the practical use of established test methods like LAL for Endotoxin testing.

You become informed about

- International regulatory developments
- Feasibility of new and innovative products and methods
- Special issues like masking/LER
- Testing of critical substances
- Application of alternative testing methods – MAT or RFC

Programme Day 1

Towards Animal Free Pyrogens Test in the Ph. Eur: Latest Progress

- Status update on the project, including information on the latest revision of chapter 2.6.30 Monocyte-activation test
- Feedback from the International Conference held in Bruxelles 14-16 February 2023: The future of Pyrogenicity testing
- Next steps towards the suppression of the rabbit pyrogens test

Dr Gwenaël Ciréfice, EDQM

If it's not Broken, why Fix it?

- Generic products with 50+ years of utilization
- Pharmacopoeial LAL Assays
- LAL and rFC Assays - comparative results
- Ways to level up LAL Assays

Jelena Novakovic Jovanovic, Galenika

Suitability of rFC-Based Endotoxin Tests: a Comparison Study Including Different Pharmaceutically Relevant Grades of Water and Product

- Numerous studies have so far investigated the performance of rFC test kits mainly using standardized/artificial samples, which are not always representative for samples used in the pharmaceutical industry and not always including a direct side-by-side performance analysis
- Comparison of the performance of the kinetic turbidimetric method (Method C), the kinetic chromogenic method (Method D) and the recombinant Factor C method (rFC) on different pharmaceutical water grades originated from routine water production systems
- Demonstrating that rFC and LAL are equivalent and comparable
- Broadened the matrix types to include product samples

Dr Ana Gonzalez Hernandez, GSK

Establishment of a rFC Assay for the Detection of Bacterial Endotoxins

- Comparison of available rFC test kits
- Development & validation of a software protocol for the existing measurement equipment
- Method suitability test based on spiked water samples
- Performance evaluation using more complex sample matrices

Dr Holger Kühn, BioChem

Novel Recombinant Cascade Reagent (rCR) as Equivalent of LAL for Sustainable BET

- A new rCR reagent developed to improve the weak point while maintaining high sensitivity that can quantify endotoxin to 0.001 EU/mL in 60 minutes
- Measuring by KCA with exactly the same operability as the conventional product
- The calibration curve iin comparison to conventional products Accuracy and Precision
- Equivalency with LAL in water samples and Excipients

Dr Hiroki Fukuchi, Fujifilm

A Validation Approach for Implementing a Sustainable, Scientifically Sound Recombinant Cascade Reagent

- Global regulators' acceptance status and expectations of Recombinant Cascade Reagent (rCR)
- Full alternative method validation approach for an rCR
- Overview of results and findings, and relevant comparability data

Jordi Iglesias, Charles River Laboratories

Seamless Software Integration allows for Complete Automation of the entire Endotoxin Testing Workflow

- Laboratory automation may include the integration of electronic batch record systems, software and hardware to enable new and more efficient processes
- By integrating an electronic batch record system along with endotoxin detection & analysis software, laboratories are able to automate their endotoxin testing workflow in ways not previously possible

- This novel approach minimizes the laboratory operator's manual steps to loading/unloading the automation hardware consumables, placing barcodes on sample vials, and interacting with the software interface
- A customer case showing the total time and error reductions will be presented

Sinéad Cowman, Lonza

Programme Day 2

Transformative Developments in Endotoxin Testing

- The latest understanding of expectations for LAL to LAL comparability
- Evaluation of comparability between novel recombinant reagents and LAL reagents
- Implementation of standardized and highly reproducible procedures for endotoxin
- How The use of recombinant reagents changed The landscape of global QC testing

Dr Veronika Wills, Associates of Cape Cod

A Trimeric Coiled-Coil Motif Binds Bacterial Lipopolysaccharides with Picomolar Affinity

- A peptide derived from a model leucine zipper binds LPS with high affiniity and no apparant off rate
- Binding is to the invariant parts of LPS; the Lipid A
- The peptide can dissolve LPS micelles
- The peptide binds lipoloysaccharides from diverse species

Prof Dirk Linke, University Oslo

All endotoxins are Lipopolysaccharides, but all Lipopolysaccharides are not Endotoxins!

- Some well-characterized and purified LPSs were used to understand endotoxins detection rules
- LPS structures vary according to the bacterial environment or to little changes in growth conditions
- The impact of LPS level of aggregation on detection, and activities, was investigated
- LAL data were compared to LC-MS2 LPS quantification, and HEK-blue TLR-4 activity

Dr Martine Caroff, LPS -Biosciences

Endotoxin Masking – Dependency on LPS Mutant and Matrix Formulation

- Correlation between LPS structures and the endotoxic potential
- Understanding of the effect of LPS structures on the mechanism of LER
- Investigations of LER with different LPS mutants and different matrix formulations
- Comparison of effect on endotoxin detection of mutants in different assay systems

Luisa Burgmaier, Microcoat

Preselection of NEP-Reference Materials in Different MAT-Setups

- MAT
- TLR ligands
- Harmonization

Josephine Hubloher, Paul Ehrlich Institut, German Federal Instituite for Vaccines and Biomedicines

Implementing New Type of Monocyte Activation Test Method to Detect and QuantifyPpyrogens

- Pyrogens
- New type of method
- Kit qualification

Dr Kasia Marciniak-Darmochwal, Charles River Laboratories

Advancing Pyrogen Testing with Automated MAT

- The Need for Automated MAT: Limitation of existing pyrogen testing methods in terms of speed, consistency, and scalability
- How automated MAT can address these issues, offering enhanced accuracy and high-throughput capabilities
- Implementation and Impact of Automated MAT
- Advancing testing procedures but also significantly impact the safety standards in the pharmaceutical and medical industries

Ruben Huis in 't Veld, MAT Research

Development of a Novel MAT test product (MylcMAT) Using Immortalized Monocyte cells (aMylc cell) Derived from Peripheral Blood Mononuclear Cells

- Generating immortalized monocyte cells from peripheral blood mononuclear cells (aMylc cell) to develop a new MAT evaluation product (MylcMAT)
- Current developments in Japan and Europe
- Resolving the concerns about stable supply with existing PBMCs Development process and Characteristics of the cells and the MylcMAT

Kazuo Miyazaki, MiCAN Technologies Inc

MAT Investigation on Two Non-Endotoxin Pyrogens

- MAT according to new EP methodology no 1
- Single donor test
- Test with pooled donors
- Comparison

Dr Peter Brügger, Lonza/MAT Research

Speakers

Dr Peter Brügger, *Lonza/MAT Research.* Senior scientific advisor.

Luisa Burgmaier, *Microcoat.* Doctoral Student.

Dr Martine Caroff, *LPS-Biosciences.* Chairwoman and CSO.

Dr Gwenaël Ciréfice, *EDQM.* Scientific Officer, European Pharmacopoeia Department.

Sinéad Cowman, *Lonza.* Director, Strategy & Market Intelligence.

Dr Hiroki Fukuchi, *Fujifilm.* Researcher/Assistant Manager.

Dr Ana Gonzalez Hernandez, *GSK.* Projekt Manager Global QC.

Dr Josephine Hubloher, *Paul Ehrlich Institut, German Federal Institute for Vaccines and Biomedicines.* Postdoctoral researcher and member of the group "Microbiological Safety" specialized on pyrogen testing.

Ruben Huis in 't Veld, *MAT Research.* Scientist Monocyte Activation Test Specialist.

Jordi Iglesias, *Charles River Laboratories.* Technology and Market Development Manager.

Dr Holger Kühn, *BioChem.* Laboratory Head Microbiology.

Prof Dirk Linke, *University Oslo.* Section for Genetics and Evolutionary Biology.

Dr Kasia Marciniak-Darmochwal, *Charles River Laboratories.* Head of Analytical Strategies and Scientific Support.

Kazuo Miyazaki, *MiCAN Technologies Inc.* Chief Executive Officer.

Jelena Novakovic Jovanovic, *Galenika.* Microbiology Manager.

Dr Veronika Wills, *Associates of Cape Cod* Associate Director, Global Technical Services.

Alternative and Rapid Microbiological Methods
21/22 November 2023

Background & Objectives

Scientific progress in the field of cell and molecular biotechnology has led to the rapid development of biopharmaceuticals, tissue engineered applications and advanced therapy medicinal products. Against this background, the safety of these new technologies, products and applications is becoming increasingly important. An important issue in the context of risk assessment and safety is contamination with microorganisms and mycoplasmas and their detection, prevention and control using rapid and appropriate methods.

In the context of this conference, current developments in the relevant regulations and scientific methods will be presented and, in addition, experiences in the implementation and validation of alternative and rapid methods will be reported. It will cover applications for in-process control as well as those used in the context of product release. Examples of real-time or online monitoring will also be regularly covered.

This conference will provide an opportunity to discuss the latest advances in technology as well as practical aspects and concerns for meeting regulatory requirements. State-of-the-art presentations by competent speakers from the authorities as well as industrial and academic experts in the field of microbiological detection and identification will provide a comprehensive overview.

Programme Day 1

Future rRevision of Ph. Eur. Chapters 5.1.6 "Alternative methods for control of microbiological quality" and 5.1.9 "Guidelines for using the test for sterility"

- Stakeholder feed-back on needs to revise 5.1.6
- Plans for future revisions to facilitate the use of rapid microbiological methods
- Rapid sterility test: how to integrate the practice in the Ph. Eur.

Dr. Solène Le Maux, EDQM

New Generation of Solid Phase Cytometry for Rapid Sterility Testing of Pharmaceutical Products (under Ph. Eur chapter 2.6.1)

- Collaboration to develop a rapid sterility test in less than 5 days
- Demonstrating its equivalence compared to traditional sterility test described in EP 2.6.1
- Results obtained on a first set of Pharmacopeia strains
- Including challenging microorganisms such as Cutibacterium acnes

Dr Joseph Pierquin/Dr Silvia Scotti, Redberry/Eurofins Biopharma Product Testing

The Route to Faster Bioburden and Sterility Testing with the Milliflex Rapid System 2.0

- Product and technology overview
- Workflow overview for bioburden & sterility testing
- Validation approach and results

Dr Anne-Grit Klees, Merck

Rapid Micro QC Test - Ensuring Product Safety When It Really COUNTS

- Current Challenges for ATMP manufacturing – A regulatory and methodology perspective
- Minimizing risk for patients and manufacturers – with rapid automated incubation and counting
- ATMP manufacturer success stories

Johannes Oberdörfer, RMB

Physical and Biological Sampling Efficiency for Active Microbial Air Samplers

- Present European and upcoming Iso standards for bioconta-mination control in pharmaceutical environments require vendor qualification of active air samplers
- The presentation will address different methods for the determination of the physical and biological sampling efficiencies
- The results gained by the different methods and for different air samplers are compared and interpreted

Dr Miriam Schönenberger, MBV

Automated Environmental Monitoring Plate Reading Powered by AI

- Overcoming Automated Plate Reader Challenges using AI
- Proof of concept and validation approach
- Future process state for EM plate reading
- Key points for Industry and Regulatory acceptance

Andrew Gravett, AstraZeneca

Building the House of Rapid Sterility - A Successful Platform Approach to introducing Rapid Methods

- Implementation of rapid sterility; using a strategic approach to reduce post-approval change burden, introduce use of rapid methods earlier in the pipeline and reduce validation time
- Overcoming business challenges with alternative methods; perception of risk, regulatory challenges and finance
- Examples of use of business cases for product on boarding and the use of rapid sterility for multiple applications

Sophie Drinkwater, Astra Zeneca

A Unique Instrument Combining Real-Time Viable Particle Counting and Traditional Growth-Based Sampling. Validation approach and results

- Introduction of a new rapid microbiological instrument that allows simultaneous 1) viable particle counting; 2) total particle counting; 3) long-term sampling on agar medium for microbial identification
- Method introduction: Use of multi-angle and timely resolved scattered light pattern analysis and fluorescence spectra measurement resolved over 16 channels, Its combination with a traditional growth-based method

- Validation approach: Explication of the simple yet robust methodology for validation of the real-time viable counting that can even be done in-house by users
- Results of primary validation: Presentation of the excellent and consistent results for real-time viable counting compared to established growth-based method

Dr Svetlana Kiseleva, Plair

Programme Day 2

Alternatives and Rapid Microbiological methods and Pharmacopeias Regulation

- US, Japan and China
- Their link to alternative methods

Dr Thierry Bonnevay, Sanofi

A Review of the Next Revision to PDA Technical Report #33

- Summarize the current TR33 and identify areas that need to be updated to reflect current industry and regulatory expectations
- Describe new and enhanced TR sections that address current validation and statistical analyses expectations.
- Discuss how ATMPs and short-shelf life products will be addressed
- Understand how the TR will address regulatory and compendial changes since the 2013 revision

Dr Michael Miller, Microbiology Consultants LLC

Primary Validation of Flow Cytometry as an Alternative Plate Count Method

- Presentation of the method and its applications
- Fundamental questions for RMMs... What do we really measure and how can the data be interpreted?
- Primary validation as the basis for further validation

Dr Jürgen Illerhaus, BWT Aqua

Next Generation Pyrogen Testing Method Developed for Rapid, ELISA Free and Variety of Pyrogen Detection

- A next generation pyrogen testing method that offers rapid, robust, and highly sensitive assay.
- However, MAT using PBMC (Peripheral Blood Mononuclear Cells) ELISA (Enzyme-Linked Immunosorbent Assay) assay raises concerns about data variability, PBMC availability, and required assay time (2 days).
- NF-kB reporter gene transfected cell lines for MAT and the cells reactivity for LPS (Lipopolysaccharide) and variety of NEP (non-endotoxin pyrogen).
- Results with LPS LOD <0.01 EU/mL and coverage for most of TLRs (Toll-like receptor).
- The advantages of NF-kB reporter gene assay

Dr Tomohisa Nanao, Fujifilm

Detection of DNase and RNase Contaminations in Pharmaceuticals and Single Use Devices. A Practical Approach of Method Validation and Development of Suitability Tests

- The Risk of Nuclease contamination in modern vaccines and ATMPs
- Kits for the rapid detection of RNase and DNase and the issue with their applicability for GMP quality control and their validation according to the current regulatory requirements
- Validaton of appropriate kits in order to transfer them into the GMP environment and enable a GMP compliant quality control
- Validation strategy, examples of suitability tests on different matrices (e.g. plastic ware)

Annemarie Jordan, Labor LS

NGS in Bacteriology: Experience with an Emerging Technology

- An overview of the available NGS platforms
- Potential use of NGS in pharmaceutical manufacturing
- Pitfalls and unsolved questions with NGS methodology

Dr Oleg Krut, Paul Ehrlich Institute, German Federal Institut for Vaccines and Biomedicines

NGS Strategies from Sample to Report for Microbial Identification and Viral Contamination Detection in Pharma

- Ion Torrent NGS Technology Overview
- GMP Compliant Genexus Integrated Sequencer System Overview
- Ion Ampliseq Technology
- Targeted and Non-Targeted Sequencing Approaches for Microbial Identification and Viral Contamination Detection

Dr Inanc Erserim, Thermo Fisher Scientific

Speakers

Dr Thierry Bonnevay, *Sanofi.* Global Microbiology Analytical Expert.

Sophie Drinkwater, *Astra Zeneca.* Senior Scientist , New Modalities and Parenterals Development, Pharmaceutical Technology & Development.

Dr Inanc Erserim, *Thermo Fisher Scientific.* Senior NGS Sales Specialist.

Andrew Gravett, *AstraZeneca.*

Dr Jürgen Illerhaus, *BWT Aqua.*

Annemarie Jordan, *Labor LS.*

Dr Svetlana Kiseleva, *Plair.* Chief Marketing Officer.

Dr Anne-Grit Klees, *Merck.* Lead Expert, Product and Portfolio Manager.

Dr Oleg Krut, *Paul Ehrlich Institute, German Federal Institut for Vaccines and Biomedicines.*

Dr Solène Le Maux, *EDQM.* Scientific Programme Manager in the European Pharmacopoeia Department.

Dr Michael Miller, *Microbiology Consultants LLC.* President.

Dr Tomohisa Nanao, *Fujifilm.* Assisstant Manager/Researcher.

Johannes Oberdörfer, *RMB.* Field Application Scientist.

Dr Joseph Pierquin, *Redberry.* Chief Technical and Scientific Officer.

Dr Miriam Schönenberger, *MBV.* Product Manager.

Dr Silvia Scotti, *Eurofins Biopharma Product Testing.* Senior Project Manager.

Cell and Gene Therapies/ATMPs – Quality and Safety
21/22 November 2023

Background & Objectives

This meeting is aimed at manufacturers and developers of cells, tissues, cell- and tissue-based products or ATMPs and deals with microbiological and analytical quality requirements, suitable methods and test systems and their implementation and validation. Representatives from authorities and colleagues from small-scale and industrial manufacturing and academic institutions will explain the current regulatory requirements and report on their experiences during inspections and implementation in the company.

Modern regenerative medicine systems such as cells and tissues or ATMPs (gene therapeutics, somatic cell-based products and tissue-based products) represent an innovative group of medicinal products that is becoming increasingly important. With the entry into force of several regulatory directives, e.g. the European Directive EC 1394/2007 for ATMPs, such products have been classified as medicinal products and as such must comply with EU requirements for medicinal products. Although the biopharmaceutical industry has significantly intensified its activities in this area, many of these products are developed and manufactured at universities, hospitals and in small and medium-sized enterprises. These university or medical roots lead to special challenges for the respective institutions as well as for the regulatory authorities in meeting compliance requirements for quality, safety and GMP aspects and approval. The frequently given manufacturing conditions also contribute to this, e.g. the open manipulation of cells and tissues necessary for obtaining such products on a medical-surgical level, or the short shelf life of the obtained end product. And potentially there are always conflicts when it comes to the relevance of different guidelines, e.g. when an Annex 1, or an Annex 2 or a WHO Guideline does not harmonise with the ATMP Guideline.

But also rapid tests and analyses are a challenge for such products with a short shelf life in terms of

- Comparability with Compendial Methods
- Sensitivity and Robustness
- Suitability Testing and Validation
- Variability

Target Audience

This conference is of interest to professionals from

- Biotechnological & Biopharmaceutical Companies
- Contract Service Laboratories
- Academic Research Institutions and Organizations
- Government Agencies
- Cell Culture Collections
- Supplier Detection Systems

with responsibilities in

- Manufacturing
- Quality Assurance
- Quality Control
- Regulatory Affairs
- Research & Development
- Process Development
- Validation

Speakers

Alicja Fiedorowicz, *Dark Horse Consulting.* Senior Consultant.

Matthias Heemskerk, *CellPoint, a Galapagos company.*
Head of Analytical Development.

Dr Sascha Karassek, *Charles River Laboratories.*
Scientist R&D Bioassay.

Dr Sabine Hauck, *Leukocare.*
EVP Corporate Development.

Dr Ferran Sanchez, *Sciex.*
Market Development, Manager, Pharma/CRO EMEA.

Dr Sebastian Ulbert, *Fraunhofer-Institut für Zelltherapie und Immunologie.* Deputy Head of Institute Head of Department Vaccines and Infection Models.

Dr Markus Fido, *MFI Consulting.*
CEO.

Dr Stefanie Bayer, *Labor LS.*
Director Molecular Development.

Dr Mahdieh Rahmatollahi, *Thermo Fisher Scientific.*
Field Application Scientist - Genetic Sciences (qPCR-dPCR).

Dr Nicole Paland, *Minerva Biolabs.*
Head Product Development.

Dr Cornelia Rosner, *Minaris.*
Team Lead Tech Transfer/Clinical Quality Control.

Olga Müller, *Tetec.*
Head QC.

Dr Ruth Röder, *Microcoat.*
Director Endotoxin Services.

Dr Christian Faderl, *bioMérieux.*
Project Leader.

Programme Day 1

Analytical Challenges in Development of Cell and Gene Therapies

- Regulatory expectation for analytical testing of ATMP
- Creation of analytical testing strategy, analytical target profile and working operational ranges
- Challenges in development, optimization and validation of assays for ATMP testing
- Example of delays to approval due to analytical testing hurdles

Alicja Fiedorowicz, Dark Horse Consulting

Challenges of a Point-of-Care Model for Cell Therapy from an Analytical Perspective

- GMP licensing
- Space constraints
- Incoming goods
- Technical skills of operators

Matthias Heemskerk, CellPoint, a Galapagos company

Potency Testing for ATMPs

- Guideline requirements for potency testing of advanced therapy medicinal products (ATMPs)
- Challenges
- Reflection of MoA
- Matrix Approach
- Validation Considerations
- Brief case studies for plasmid and LNP products

Dr Sascha Karassek, Charles River Laboratories

Analytical Methods to Support mRNA-LNP Formulation Development

- Method selection based on USP guidelines and literature
- Aligning CQA with suitable analytical methods
- Analytical data for the selected toolbox

Dr Sabine Hauck, Leukocare

Achieve Lower LLOQs for siRNA Quantification in Plasma Using Microflow LC

- Overcome the difficulties of analyzing oligonucleotides using microLC
- Easy transfer of high flow LC to microLC
- Get extra level of sensitivity thanks to the combination of a high end triplequadrupole with microLC

Dr Ferran Sanchez, Sciex

Analysis of Radiation-Inactivated Pathogens for Vaccine Development (LEEI)

- Low energy irradiation (LEEI) is a novel method for the production of inactivated vaccines, with several advantages over chemical inactivation
- Pathogens treated with LEEI largely maintain their surface antigens
- Downstream analysis includes verification of inactivation and antigenicity testing

Dr Sebastian Ulbert, Fraunhofer-Institut für Zelltherapie und Immunologie

Different Analytical Tools to characterize ATMPs - from Assay Development to Release Testing

- Different therapeutics – different analytical methods
- Differences during product development – which level is necessary at which stage?
- Regulatory needs versus internal needs for characterization – mandatory or nice to have?
- Product release & stability studies – and their specification
- Examples of dedicated methods – high end discussion & alternatives

Dr Markus Fido, MFI Consulting

Selection of Appropriate Methods for Detection of Microbiological Contaminations in ATMPs

- Shelf life of many ATMPs is usually short (one to five days); in addition, many ATMPs are derived from cells and tissues.
- For ATMPs with a shelf life of three to five days, several methods are available.
- For ATMPs with an even shorter shelf life of approximately one day, just a few are available for cell based products.
- In the presentation data is shown achieved by using rapid ATP bioluminescence for standard rapid tests and qPCR for ultra rapid testing.

Dr Stefanie Bayer, Labor LS

Programme Day 2

Innovations in Quality Control for Cell and Gene Therapy using Digital PCR

- Feasibility of determining AAV genometiter,
- Evaluating AAV Genome Integrity on dPCR using linkage analysis
- Calculating full/empty capsid ratio using multiplex data on dPCR
- Choosing the right technology for product safety and quality (e.g. resDNA)
- Update on regulatory guidelines for dPCR

Dr Mahdieh Rahmatollahi, Thermo Fisher Scientific

Development of a Digital PCR-Based System for the Detection of Residual DNA in Pharmaceutical Products

- Residual DNA - the presence of DNA fragments from a host organism in the final product from recombinant biological processes
- Safety concern due to their associated increased oncogenicity, infectivity, and immunogenicity
- Regulatory Limits
- Digital PCR (dPCR)as a higher sensitive system in comparison to the golden standard qPCR
- Three dPCR-based detection kits for the detection of residual DNA impurities in pharmaceutical products manufactured in Escherichia coli, Chinese hamster ovary cells (CHO) or HEK293 human cells

Dr Nicole Paland, Minerva Biolabs

Mycoplasma Testing & Evaluation for ATMPs – Lessons Learned!

- Comparison of SYBR-Green based and probe-based assay
- Challenges in method development & analysis
- Troubleshooting
- Method validation of a probe-based assay

Olga Müller, Tetec

Transfer of Complex Analytical Methods for ATMPs

- Technology transfer framework
- Concept and modes of tech transfer
- Applications and implications for complex analytical methods
- Case studies

Dr Cornelia Rosner, Minaris

Challenges of Endotoxin Detection During Development of a Novel product

- Presentation of a case study for identification of an analytical method for the quantification of endotoxin associated with a novel immunotherapeutic virus-like particle (VLP), where intrinsic endotoxin contamination is expected
- Demonstration how development of novel drug products can raise new challenges for endotoxin testing
- Comparison of BET and MAT testing for this new product
- Overcoming BET limitations for this product with MAT

Dr Ruth Röder, Microcoat

Automating the Future of Cell and Gene Therapy: Streamlining Endotoxin Detection, Data Integrity and Compliance Solutions with recombinant Factor C

- he interest of a highly specific endotoxin detection assay based on ELISA-technology and recombinant Factor C (rFC) to overpower the C&GT product interferences.
- he advantages of semi- and full automation of endotoxin testing for the streamlining of the cell and gene therapy quality control program
- High throuput full automated endotoxin testing with data integrity
- How to achieve compliance (EP and USP chapters for endotoxin testing update, Annex 1 overview for data integrity)

Dr Christian Faderl, bioMerieux

The Social Event

On the evening of the first congress day, on 21 November 2023, all congress delegates and speakers are invited to a „Get together" in the Congress Center. Take advantage of this opportunity for an information exchange and enjoy the laid-back atmosphere and the entertainment programme.

PharmaLab Exhibition

Parallel to the conferences, participants will have the opportunity to visit the accompanying trade exhibition. It offers comprehensive information about available products, services and the latest developments around the laboratory.

All details at:

www.pharmalab-congress.com/exhibitors-plan.html

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A one-day ticket/two-day ticket will enable you to visit the congress (21 November/22 November 2023) either only on day 1 or only on day 2 or on both days. The charges for the one day tickets are € 690,- plus VAT, for the two days ticket € 1.380*,- plus VAT. They include lunch and beverages during the conferences and in breaks as well as the social event on the evening of the first congress day (Due to the special fees for the congress, ECA membership discounts are not applicable).
The visit of the pre-conference on 20 November 2023 for € 590,- can be combined with the congress (see registrations options on the last page). Charges are payable after receipt of invoice.

The Social Event

On the evening of the first congress day, on 21 November 2023, all congress delegates and speakers are invited to a „Get together" in the Congress Center. Take advantage of this opportunity for an information exchange and enjoy the laid-back atmosphere and the entertainment programme.

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Registration Options PharmaLab 2023

I want to take part in:

- ☐ PharmaLab Pre-Conference Workshop "4th International Mycoplasma qPCR Testing User Day" (20 Nov 2023) - € 590,- plus VAT
- ☐ PharmaLab Conferences on 21 Nov 2023 – € 690,- plus VAT (until 31 August)
- ☐ PharmaLab Conferences on 22 Nov 2023 – € 690,- plus VAT (until 31 August)
- ☐ PharmaLab Conferences on 21 and 22 Nov 2023 – € 1,380,- plus VAT (until 31 August)

With a one-day ticket/two-day ticket for the PharmaLab Conferences (21 Nov/22 Nov 2023) you can attend any conference offered that day/both days. It includes the visit of the exhibition. In addition, it comprises lunch and beverages during the conferences and in breaks (on one or both days) as well as the social event on the evening of the first congress day. Please mark if you would like to attend the Social Event.

☐ Yes, I would also like to take part in the Social Event on the evening of 21 November. ☐ No

To be able to prepare the conference rooms, we would appreciate it if you marked the conference you are interested in. Please also mark the day you plan on attending the Congress. **Please mark only one conference per day.**

☐ I would like to attend on **day 1 (21 November 2023)** and I'm primarily interested in the conference:

- ☐ ECA – GMP Compliance Trends in Analytical Laboratories/Outsourcing in Pharmaceutical Laboratories
- ☐ ECA – Analytical Method Validation and Life Cycle Management - ICH Q14/Q2 (R2) (Day 1)
- ☐ ECA – Endotoxin and Pyrogen Testing (Day 1)
- ☐ ECA – Alternative and Rapid Microbiological Methods (Day 1)
- ☐ ECA – Cell and Gene Therapies/ATMPs - Quality and Safety (Day 1)

☐ I would like to attend on **day 2 (22 November 2023)** and I'm primarily interested in the conference:

- ☐ ECA – Laboratory Optimization, Automation and Digitalization
- ☐ ECA – Analytical Method Validation and Life Cycle Management - ICH Q14/Q2 (R2) (Day 2)
- ☐ ECA – Endotoxin and Pyrogen Testing (Day 2)
- ☐ ECA – Alternative and Rapid Microbiological Methods (Day 2)
- ☐ ECA – Cell and Gene Therapies/ATMPs - Quality and Safety (Day 2)

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