A Joint Workshop of the
Paul-Ehrlich-Institut (PEI) and ECA

Monocyte Activation Test – MAT

Use and Implementation of MAT

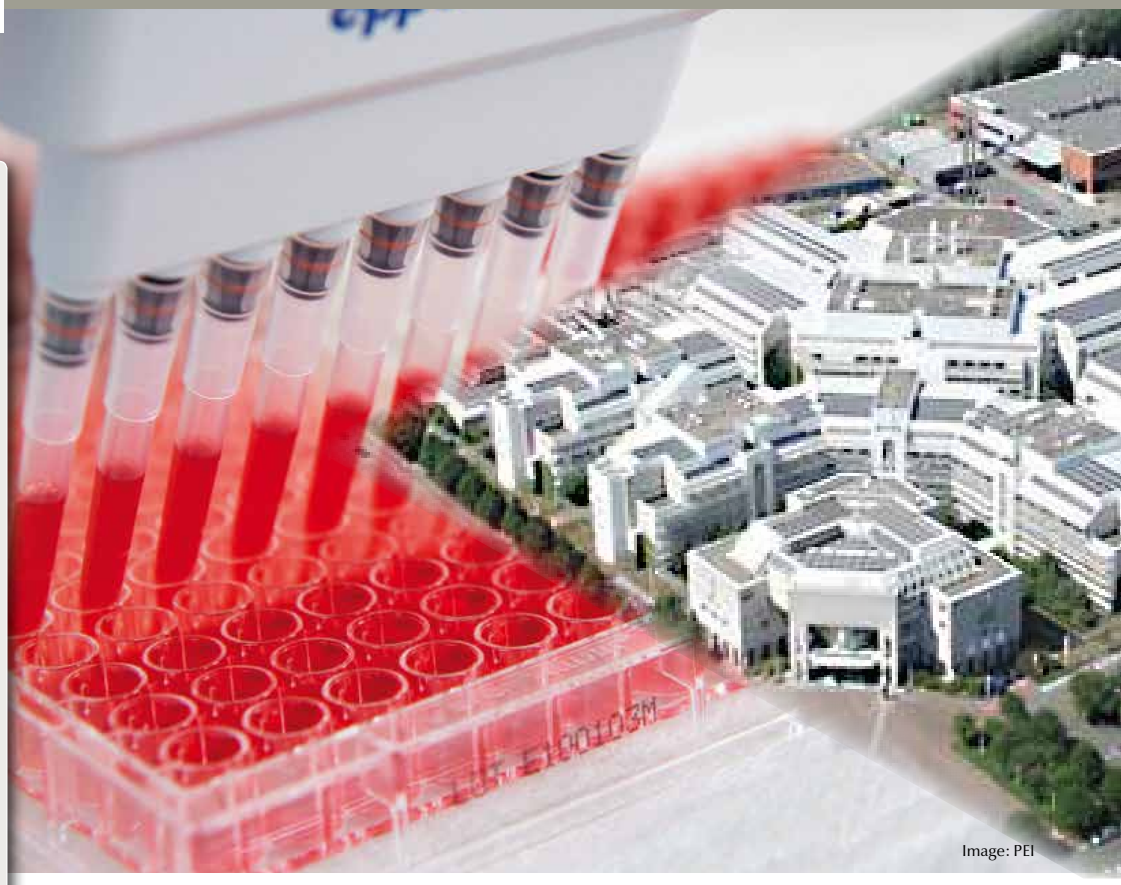
Image: PEI

Speakers from Authorities

DR KLAUS CUSSLER
Paul-Ehrlich-Institut, Germany

DR INGO SPREITZER
Paul-Ehrlich-Institut, Germany

DR DON SINGER
USP, USA

DR KARIN NORDGREN
NIBSC

Speakers from Industry and Science

KRISTIN KOWALICK
Labor L+S AG, Germany

DR ANJA FRITSCH
Confarma, France

DR KATARZYNA MARCINIAK-DARMOCHWAL,
Charles River Laboratories, Ireland

DIPL ING MAIKE PIEHLER
Microcoat, Germany

DR ASTRID VISSER
Sanquin, The Netherlands

DR WALTER ZWISLER
Zwisler Laboratory, Germany

10th Anniversary of ECA's Rapid Microbiological Methods Group

7 September 2016, Frankfurt/Langen, Germany

Join us at the pre-workshop **Get-Together** on 6 September in the Steigenberger Hotel Frankfurt-Langen

HIGHLIGHTS:

- Regulatory Background in Europe and US
- Status Report on the Development, Validation and Regulatory Acceptance of Alternative Methods and Approaches
- Use of Cell Lines
- Advantages and Pitfalls
- MAT - Batch release of modern vaccines

This conference is recognised for the ECA GMP Certification Programme „Certified Microbiological Laboratory Managerr".
Please find details at www.gmp-certification.eu

Monocyte Activation Test – MAT

06 and 07 September 2016, Frankfurt/Langen, Germany

Invitation

Dear Colleagues,

The first workshop on MAT was held at the Paul-Ehrlich-Institute on 22 November 1999, so to say in the last Millennium. This was my first visit to the PEI (still working on my PhD thesis in Constance), the icy weather caused many accidents and obstacles on the road.

Since then we have seen a lot of obstacles hindering the widespread implementation of the MAT, although during the last 17 years an enormous effort and progress was achieved by several esteemed partners within the community.

The European validations (together with ECCVAM) were finalized and accepted successfully. With continuous support by the German Pharmacopeia, the EDQM MAT Expert group was re-established and finally the MAT Monograph 2.6.30. was implemented into the European Pharmacopeia in 2010. Meanwhile, the EDQM performed an MAT survey to improve the MAT monograph. The BET Guideline 5.1.10. and the Rabbit Pyrogen Test (RPT) monograph 2.6.8. have been revised to clarify the priorisation of the MAT compared to the RPT (especially in regard to the EU Directive 2010/63). Furthermore, the microbial safety unit at the PEI discontinued the RPT at the end of 2014, thus highlighting the significance of the MAT.

In a series of workshops and conferences MAT experts shared their thoughts with those who were interested and/or affected by these developments.

Finally, after more than 20 years, we have reached a point where we have to do what we worked for all the time: Replacing a good and predictive animal test with an even better alternative method.

The purpose of this workshop is to provide the participants with guidance and support for the upcoming changes, a vision which both the PEI and the ECA share. Experts from Authority, Industry and Contract Laboratories will provide insight into their experiences with the implementation of MAT.

With best regards,
Dr Ingo Spreitzer, PEI

Background

During recent years manifold advances have taken place to replace both, Rabbit Pyrogen Test (RPT) and in some cases the Limulus Amebocyte Lysate Test (LAL).

Some of the reasons are:

- Animal experiments have to be reduced. Especially with the current EU Regulations. Also the LAL test is not a true in vitro test.
- Get an alternative Test, where the classic LAL shows some gaps, e.g. contamination of biologicals by non-endotoxin pyrogens not detectable in LAL test is not unlikely.
- LAL reagent has to be harvested from Horseshoe Crabs. An environmental or an ecological disaster could extinguish the Limulus population.

True In-vitro Pyrogen Tests (IVPT) have been developed in several European countries (United Kingdom, The Netherlands, Switzerland, Germany) in national and international research projects. The tests imitate the central step of human fever reaction, i.e. the activation of human monocytes by endotoxin as well as non-endotoxin pyrogens. One result of all these activities is the Monocyte Activation Test (MAT).

This unique event is jointly organised by the Paul Ehrlich Institut – Federal Institute for Vaccines and Biomedicines and the ECA Academy to bring together European industry and regulatory representatives in order to discuss the practical experiences in using MAT, the advantages, the pitfalls, the available systems as well as the regulatory experiences.

Target Audience

This workshop is addressed to all persons of

- pharmaceutical manufacturers, biopharmaceutical companies, medical device manufacturers, contract laboratories, tissue establishments, and authorities

who are involved in Endotoxin and Pyrogen testing in development, IPC or release.

Moderator/ Chair

Dr Isabell Bekeredjian-Ding, PEI and member of the Microbiology Group Advisory Board and
Dr Sven Deutschmann, Roche Diagnostics, Chair ECA Pharmaceutical Microbiology Working Group

Programme

Current Developments on MAT
- Drivers for MAT-related pharmacopeial changes: Users and EU Directive
- The interaction of 5.1.10., 2.6.8. and 2.6.30.
- MAT availability
- PEI position on MAT

DR INGO SPREITZER, PEI

USP Requirements and Regulatory Thinking
- Current Regulatory Background
- Expected Developments

DR DON SINGER, USP

Implementation of Alternatives to Animal Safety
- History – the Issue of solving Salvarsan "Sodium Chloride/Water Fever"
- Development of JEG 3R (replacement, reduction, refinement)

DR KLAUS CUSSLER, PEI

MAT – Pitfalls and Lessons learned
- MAT - one test various test procedures
  - Pros & cons from the perspective of a contract laboratory
- Critical aspects of the test
  - Blood source
  - Realization of the Ph.Eur. requirements: 4 Replicates, LOD
- Summary: Points to consider for the routine use of MAT

KRISTIN KOWALICK, L+S AG

MAT using cryopreserved pooled PBMCs
- MAT as pyrogen test
- Characteristics and Performance of MAT assay of Sanquin
- Examples of validation and drug release testing of plasma derived products
- Critical aspects and tips for performing MAT

DR ASTRID VISSER, SANQUIN

MAT use for Medical Devices
- Medical Devices vs pharmaceutical samples
- Pooled human cryoblood experience

DR WALTER ZWISLER, ZWISLER LABORATORIUM

MAT Testing with Monomac6 Cell Line
- Advantages of performing the MAT in a routine Laboratory using a cell line
- Assay characteristics
- Experiences with validations and routine testing

DR ANJA FRITSCH, CONFARMA

Experiences with MAT
- Evaluation of a one-step MAT assay
- Feasibility data using various pyrogen
- Validation concept for MAT as a generic pyrogen test

MAIKE PIEHLER, MICROCOAT

MAT Batch Release of Modern Vaccines
- OMV-based vaccines and pyrogen testing
- MAT-approach for batch release

DR KARIN NORDGREN, NIBSC

Overcoming the Challenges in Establishing Routine MAT Assay
- The MAT assay and testing of different sample/product types
- A look at the types of interference that may be seen with the assay
- Controlling the robustness of the MAT assay

DR KATARZYNA MARCINIAK-DARMOCHWAL, CRL

Speakers

DR KLAUS CUSSLER,
Paul-Ehrlich-Insitut, Federal Institute for Vaccines and Biomedicines
Dr Cussler studied Veterinary Medicine at the University of Mainz. He is a specialist in Veterinary Microbiology and Animal Welfare. Since 1987 he is Head of Veterinary Pharmacovigilance at the Paul-Ehrlich Institut.

DR ANJA FRITSCH,
Chief Scientific Officer, Confarma France Sarl, Molecular Biology, France
Anja Fritsch gained her PhD in 2004. After a post-doc period at the University of Freiburg, she joined Confarma in 2011 as Chief Scientific Officer. Her main field of interest is the development of cell-based assay systems for the analysis of variety of biological reactions.

KRISTIN KOWALICK,
Labor L+S AG, Germany
Kristin is a biologist by training and is Head of the R&D laboratory at L+S AG. The responsibility of this lab is the evaluation, testing and validation of new customized microbiological methods.

DR KATARZYNA MARCINIAK-DARMOCHWAL,
Charles River Laboratories, Ireland
Katarzyna studied Biology at the University of Warmia and Mazury. After 4 years as academic teacher and research technician, she joined Lonza Biologics at Slough in 2007. From 2012 – 2015 she worked for UCB as Senior Method Development and Validation Scientist. 2015 she came to CRL as Senior Project Leader Method Development Department.

DR KARIN NORDGREN,
NIBSC, Medicines and Healthcare Products Regulatory Agency, UK
In her current position, Karin works at the Biotherapeutics Group of the National Institute for Biological Standards and Control.

DIPL ING MAIKE PIEHLER,
Microcoat Biotechnology GmbH, Germany
Maike studied Biotechnology in Hamburg. After different positions in product development at Hyglos and quality management at Microcoat, she is currently the head of the department "Service Endotoxin Detection" at Microcoat.

DR DONALD C. SINGER,
USP Microbiology Committee, Vice-Chair, USA
Donald C. Singer is a graduate of Boston University and University of Dayton. He is a member of the USP Microbiology Committee of Experts and is Global Lead Manager, Microbiology R&D for GlaxoSmithKline. He is a Certified Specialist Microbiologist in Consumer and Industrial Microbiology and has been a Malcolm Baldrige National Quality Award Examiner.

DR INGO SPREITZER,
Paul-Ehrlich-Institut, Germany Agency for Vaccines and Biomedicines, Germany
Ingo Spreitzer studied Biology at the University of Mainz, Germany, and was awarded a doctorate in 2000. Since 2001 he has been working as a scientist at the Paul-Ehrlich-Institut. In October 2004 h was appointed Deputy head of Section 1/3, "Microbial Safety and Parasitology". Duties: Pyrogen testing (rabbit and alternatives), LAL Testing.

ASTRID VISSER,
Sanquin Plasma Products, The Netherlands
Astrid studied Biology at the University of Amsterdam and held a PhD in Medicine. After a time as postdoc she joined Phillips for several years as clinical scientist and later as project leader. 2012 she start working for Sanquin. Her current position is Business Development Manager Sanquin Reagents, project leader MAT development.

DR WALTER ZWISLER,
CEO of Zwisler Laboratorium GmbH, Germany
Dr Walter Zwisler studied Biology at the University of Konstanz and got his PhD at the University of Oldenburg. Since 2003 he is deeply involved in the In vitro Pyrogen Testing with human cryo and fresh blood. With government-funded research projects and several thousand tested samples (medical devices and pharmaceutical samples) the Zwisler Lab is well versed with the MAT.

The **Paul-Ehrlich-Institut** is the Federal Institute for Vaccines and Biomedicines. It is a senior federal authority in the field of medicinal products providing services in public health.

The Paul-Ehrlich-Institut assesses and monitors the benefit - risk balance before, during and after the marketing authorisation of biomedicines for human use and immunological medicines for veterinary use.

The Paul-Ehrlich-Institut's own experimental research in the field of life sciences is an indispensable basis for the fulfilment its duties. The Paul-Ehrlich-Institut reports to the German Federal Ministry of Health (Bundesministerium für Gesundheit).

The **ECA Foundation** is the leading European organisation with regard to pharmaceutical Quality Assurance and GMP compliance.

The goals of the ECA Foundation are still the same as follows:

- to facilitate the exchange of information between representatives of the industry, the medicines authorities and the universities in the field of pharmaceutical quality assurance, especially with regard to the area of Good Manufacturing Practice (GMP)
- to promote the move towards a harmonised set of GMP and regulatory guidelines, by providing information and interpretation of new or updated guidances,
- and to issue position papers where appropriate to influence and harmonise regulations and to facilitate networking.

The Foundation is comprised of an educational organisation (ECA Academy) and various non-profit interest and working groups. The modern structure of the ECA Foundation allows to develop and include the activities of these groups and to have more flexibility to build new groups that support the needs of our ECA Academy's members. Close to 4,000 members in the Foundation's educational organisation ECA Academy from all over Europe and abroad represent more than 60 countries.

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We look forward to welcoming at one of our next events – and we already wish you a pleasant flight!

*Please note: You may have to enable pop-ups on the Mobility Partner Program website – other-wise the booking platform window will not open.

Easy Registration

Reservation Form:
CONCEPT HEIDELBERG
P.O. Box 10 17 64
69007 Heidelberg, Germany

Reservation Form:
+ 49 6221 84 44 34

e-mail:
info@concept-heidelberg.de

Internet:
www.gmp-compliance.org

Date
Get-Together in the Steigenberger Hotel Frankfurt-Langen on
Tuesday, 06 September 2016,
18.30 h – approx. 21.30 h

Workshop at PEI on
Wednesday, 07 September, 09.30 – 16.30 h
(Registration and coffee 09.00 – 09.30 h)

Venues
Get-Together and overnight stays:
Steigenberger Hotel Frankfurt-Langen
Robert-Bosch-Str. 26
63225 Langen/Frankfurt, Germany
Phone +49 (0)6103 972 0
Fax +49 (0)6103 972 555
For hotel guests, the Steigenberger Hotel offers a free of charge shuttle service from Frankfurt Airport to the hotel (approx. 16 km distance)

Workshop:
Paul-Ehrlich-Institut
German Federal Institut for Vaccines and Biomedicines
Paul-Ehrlich-Straße 51-59
63225 Langen, Germany
Phone +49 (0)6103 770

Fees (per delegate plus VAT)
ECA Members € 690
APIC Members € 740
Non-ECA Members € 790
EU GMP Inspectorates € 395
Academics (Students, Post docs etc.) € 395
The conference fee is payable in advance after receipt of invoice and includes conference documentation, Get-Together on the evening before the workshop, and on 7 September lunch and all refreshments. VAT is reclaimable.

Conference Language
The official conference language will be English.

Accommodation
CONCEPT HEIDELBERG has reserved a limited number of rooms in the conference hotel. You will receive a room reservation form when you have registered for the conference. Reservation should be made directly with the hotel. Early reservation is recommended.

Organisation and Contact
ECA has entrusted Concept Heidelberg with the organisation of this event.

CONCEPT HEIDELBERG
P.O. Box 10 17 64
69007 Heidelberg, GERMANY
Phone +49 (0) 62 21/84 44-0
Fax +49 (0) 62 21/84 44 34
E-mail: info@concept-heidelberg.de
www.concept-heidelberg.de

For questions regarding content:
Mr Axel Schroeder (Operations Director) at +49-62 21/84 44 10 or per e-mail at schroeder@concept-heidelberg.de.

For questions regarding reservation, hotel, organisation etc.:
Ms Nicole Bach (Organisation Manager) at +49-62 21/84 44 22 or per e-mail at bach@concept-heidelberg.de.

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Monocyte Activation Test – MAT
7 September 2016, Frankfurt/Langen, Germany

☐ Yes, I will also take part in the **Get-Together on 6 September 2016** at the Steigenberger Hotel Frankfurt-Langen

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